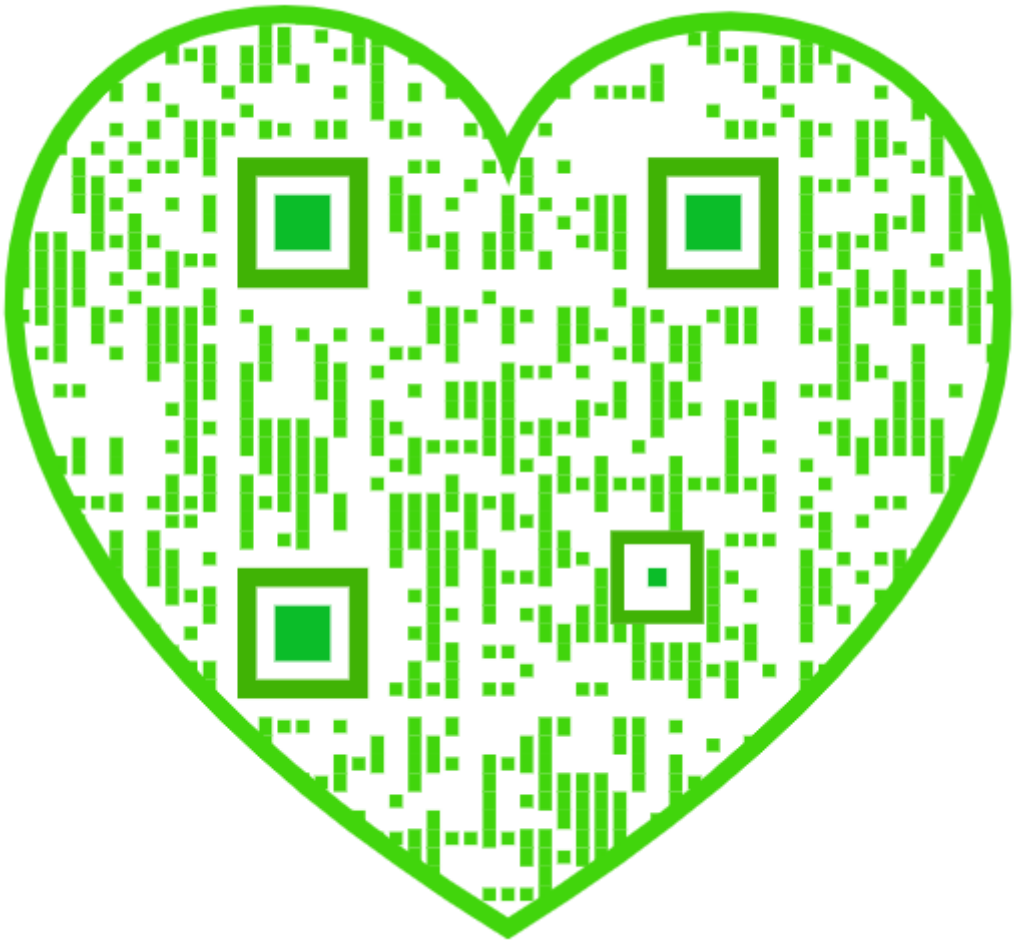

A TREATISE

ON

PHARMACY

FOR

STUDENTS AND PHARMACISTS

BY

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FIFTH EDITION, ENLARGED AND REVISED

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PREFACE TO THE FIFTH EDITION.

THE completion of the Ninth Revision of the United States Pharmacopœia and the Third Revision of the *National Formulary* have made necessary a thorough revision of the Treatise of Pharmacy in order to bring to the attention of students, in proper form, the many additions and changes involved.

The general plan of the book, which has been approved by many teachers, remains the same, as the author has been repeatedly assured that his efforts to answer, as far as possible, the many questions naturally presented to the mind of the student and the practising pharmacist as to the why and wherefore of official directions and tests, are appreciated. Much new matter has been added and a large portion of the book has been entirely rewritten with the view of bringing the various subjects under discussion up to date.

The author desires to say that the Treatise of Pharmacy is not intended as a substitute for the Pharmacopœia and the *National Formulary*, but as a guide to the intelligent study and use of these two authorities, and for that reason the insertion of fofficial ormulas and directions has been omitted, except insofar as the introduction of parts thereof may have seemed necessary for a satisfactory explanation.

As heretofore the subjects treated in this book have been grouped under three distinct headings.

Part I comprises General Pharmacy, which includes the study of weights and measures, specific gravity, the application and control of heat, mechanical subdivision of drugs, and methods of solution and separation, together with a classification and description of the various plant products and solvents used in pharmacy.

Part II treats of Practical Pharmacy. This involves a study of the official galenical preparations, together with the many operations of the dispensing counter. It has been the author's aim to explain as clearly as possible the various processes and apparatus met with in this department, and to point out the difficulties likely to be encountered, as well as the remedies therefor. All suggestions made

have been tried and verified by the author before offering them, so that statements made are based on actual experience.

Part III is devoted to Pharmaceutical Chemistry, the study of which is of paramount importance to every student of pharmacy. While the subject is a very comprehensive one, and undoubtedly entitled to an extensive treatise, it has been confined, in this work, to such compounds as are either officially recognized in the United States Pharmacopœia or are of special interest to pharmacists.

Conscious of the fact that imperfections must of necessity exist in a treatise covering so extended a field of study, the author desires to express his grateful appreciation of the favorable comment accorded previous editions of this book, and hopes that in its revised form it may prove even more closely adapted to its purposes above stated.

C. C., JR.

BALTIMORE, 1916.

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PART I.

GENERAL PHARMACY.

CHAPTER I.

PHARMACOPŒIAS.

ALTHOUGH the term *Pharmacopœia* (from the Greek φάρμακον, medicine, and ποιεῖν, to make) is defined by lexicographers as meaning a book of formulas or directions for the preparation of medicines, the word has now received a more liberal construction, and is taken to include, besides the foregoing, also descriptions of vegetable as well as mineral and animal drugs, together with appropriate tests for establishing the identity and quality of the same, the whole prepared by some recognized authority.

The necessity for a definite and authoritative standard in the selection and preparation of medicines was long since recognized by all civilized nations; thus the London Pharmacopœia was established in 1618, that of Paris in 1639, and that of Edinburgh in 1699. The first truly national standard was that of France, issuesd in 1818, which retained the name of its predecessor, the Paris Pharmacopœia, and is even today still known as the Codex Medicamentarius. The first United States Pharmacopœia was established in 1820, prior to which time various foreign pharmacopœias had been in use in this country. The British Pharmacopœia, into which were merged the London, Edinburgh, and Dublin (established 1807) Pharmacopœias, was first issued in 1864; while Germany did not adopt a national standard until 1872, nearly two years after the restoration of the German empire. Owing to the rapid advances in the science of medicine and pharmacy, frequent revisions have become necessary, and the following table shows the dates of the last revised editions of the pharmacopœias of leading nations:

Country.	Date of issue.	Country.	Date of issue.
United States	1916	Sweden	1908
Great Britain	1914	Denmark	1907
Norway	1913	Switzerland	1907
Germany	1910	Austria	1906
Russia	1910	Belgium	1906
Hungary	1909	Japan	1906
Italy	1909	Netherlands	1905
France	1908	Spain	1905
		Mexico	1904

The Pharmacopœia of the United States, as now published, represents the joint work of the medical and pharmaceutical professions; but in the early part of the last century, when pharmacy had not yet reached the state of a fully developed profession in this country, the apothecary held a rather subordinate position, and therefore had no voice in the compilation of the first national Pharmacopœia, which was adopted in 1820 by a convention of physicians assembled at Washington, D. C., under the presidency of Dr. S. L. Mitchill, the publication of the book being entrusted to a special committee, of which Dr. Lyman Spalding was chairman, and both the Latin and English languages being used in the text. In 1830, through some misunderstandings and consepuent dissatisfaction, two separate conventions were held for the revision of the Pharmacopœia, one in New York and one in Washington, and at the latter the Government medical service was represented for the first time and participated in the proceedings; at this time provision was also made for regular subsequent revisions every ten years. Owing to this confusion two distinct Pharmacopœias were published, one in 1830 in New York City, bearing the imprint "By the authority of the General Convention for the Formation of the American Pharmacopœia, held in 1830;" the other, published by authority of the National Medical Convention held at Washington, A. D., 1830, was issued in Philadelphia in 1831. In the Pharmacopœia of 1840 the Latin version of the text was omitted, and in this revision material aid was also given by the pharmacists, although they had no representation in the convention; numerous improvements in the working formulas appear in this edition. In the convention of 1850 two colleges of pharmacy were duly represented by delegates, and from this time forward the value of pharmaceutical collaboration has been recognized, and its influence is discernible in the many practical details of the Pharmacopœia. Since 1850 the convention for the revision of the Pharmacopœia has assembled in the city of Washington, D. C., regularly in the month of May of every tenth year; all duly incorporated medical and pharmaceutical societies and colleges throughout the United States are entitled to representation by three delegates, the three branches of the Government medical service being also represented by one delegate each. Until recently the final revision of the Pharmacopœia, under instructions from the convention, was entrusted to a special committee of twenty-five members, who formerly also had charge of the publication of the book; of this committee, the late Charles Rice was chairman from May, 1880, until his death on May 13, 1901.

In May, 1900, on the occasion of the national convention for the eighth decennial revision of the United States Pharmacopœia, the assembled body was incorporated under the name "The United States Pharmacopœial Convention," and the business management and control of the affairs of the convention, including the publication

of the Pharmacopœia, were placed in the hands of a board of five trustees. At this time also the introduction of average approximate doses to be stated after each pharmacopœial article was adopted.

At the decennial gathering of the convention in May, 1910, the membership of the committee of revision was increased from twenty-five to fifty and its name changed to the General Committee of Revision, from which number were appointed fifteen subcommittees, to each of which was assigned a special part of the Pharmacopœia text, thus: assay methods; cerates, ointments and plasters; extracts, fluid-extracts and tinctures; inorganic chemicals; nomenclature; organic chemicals, posology, volatile oils, etc. The chairmen of the various subcommittees constitute an Executive Committee, which has immediate charge of the work of revision. The general committee of revision, elected in 1910, consists of 11 physicians, 13 chemists, 20 pharmacists and teachers of pharmacy, 5 teachers of botany and pharmacognosy, and 1 wholesale druggist, of which body Joseph P. Remington was chosen chairman. James H. Beal was elected chairman of the newly elected board of trustees. At this meeting the following were also admitted as members of the corporation: The Secretary of Agriculture, the Secretary of Commerce and Labor, the Association of Official Agricultural Chemists, the Association of State and National Food and Dairy Departments, the National Wholesale Druggists' Association, and the National Dental Association. A series of general principles was adopted for the guidance of the general committee of revision, among which was a recommendation to state in the Pharmacopœia a range of volume content of absolute alcohol for each preparation containing alcohol, and another to admit biologic tests and assays when accurate and reliable.

Prior to 1906 the Pharmacopœia of the United States was without the power of legal enforcement by act of Government, but has since been adopted by the Congress as a standard in the enforcement of the Pure Food and Drugs Act of 1906, which controls the sale of drugs and chemicals in interstate commerce, the District of Columbia, and the territories. For many years it has been recognized as the standard employed in the purchase of medical supplies for the Army, Navy, and Marine Hospital Service of the United States, and has also been adopted in nearly all the States as the legal standard in the enforcement of laws regulating the practice of pharmacy and measures pertaining to pure food and drugs.

In 1909 a Spanish translation of the United States Pharmacopœia was published by the Board of Trustees, primarily for use in our insular possessions; this has been very favorably received by the countries of Central and South America, and has already replaced the Spanish Pharmacopœia in the Republic of Cuba as the official guide and standard of that country. The translation was made by Prof. José G. Diaz of the University of Havana.

The Pharmacopœia in use at present was published in 1916 and is known as the Ninth Revision.

As the Pharmacopœia is in almost daily use by the pharmacist, a short study of its plan and arrangement is desirable for a more intelligent understanding of the text. The titles of all drugs recognized in the Pharmacopœia, whether derived from the vegetable, mineral, or animal kingdom, are conveniently given in three subdivisions, known as the *official Latin name*, the *official English name*, and the *official definition*, to which is added an official description, by means of which the identity of all official substances can be readily established. The following examples will serve to illustrate the arrangement of pharmacopœial subjects:

PODOPHYLLUM. (Official Latin name.)

PODOPHYLLUM. (Official English name.)

Podoph. (Official abbreviation.) Mandrake, May Apple Root. (Synonyms.)

The dried rhizome and roots of *Podophyllum peltatum* Linné (Fam. *Berberidaceæ*), yielding not less than 3 per cent. of resin. (Official definition.)

Rhizome horizontal, nearly cylindrical, jointed, compressed on the upper and lower surfaces, sometimes branched; in pieces from 3 to 20 cm. in length, the internodes from 2 to 9 mm. in diameter; externally dark brown, longitudinally wrinkled or nearly smooth with irregular, somewhat V-shaped scars of scale leaves, nodes annulate, upper portion marked with large, circular depressed stem-scars and sometimes with buds or stem-bases; at or near the nodes on the lower portion occur numerous root-scars or roots from 2 to 7 cm. in length and about 2 mm. in thickness; fracture short; internally bark light brown, wood with small yellowish, vascular bundles, pith large and white; odor slight; taste sweetish, disagreeably bitter and acrid.

Under the microscope a transverse section of the rhizome of podophyllum shows an outer layer of one or two rows of reddish-brown cells; parenchyma of cortex and pith with numerous single, spherical, polygonal, or 2- to 6-compound starch grains, or rosette aggregates of calcium oxalate; vascular bundles from 24 to 34, arranged in a circle between cortex and pith. (Official description.)

The powder is light brown, with a pronounced and characteristic odor; starch grains numerous, spherical, polygonal or 2- to 6-compound, the individual grains from 0.003 to 0.15 mm. in diameter; calcium oxalate crystals few, in rosette aggregates from 0.05 to 0.08 mm. in diameter and occasionally in raphides from 0.03 to 0.09 mm. in length; tracheæ with simple pores or reticulate thickenings; fragments of starch-bearing parenchyma and reddish-brown cork cells.

Podophyllum yields not more than 3 per cent. of ash.

Proceed as directed for the preparation of Resina Podophylli, using 10 Gms. of Podophyllum in No. 60 powder. It shows not less than 3 per cent. of resin. (Assay.)

MAGNESII SULPHAS. (Official Latin name.)

MAGNESIUM SULPHATE. (Official English name.)

Mag. Sulph. (Official abbreviation.) Epsom Salt. (Synonym.)

It contains not less than 48.59 per cent. not more than 53.45 per cent. of anhydrous magnesium sulphate corresponding to not less than 99.5 per cent. of the crystallized salt ($MgSO_4+7H_2O$ = 246.50). (Official definition.)

Magnesium Sulphate occurs as small, colorless, prismatic needles, or rhombic prisms, without odor, and having a cooling, saline, and bitter taste; slowly efflorescent in the air. One Gm. of Magnesium Sulphate dissolves in 1 mil. of water at 25° C.; also in about 0.2 mil. of boiling water; almost insoluble in alcohol at 25° C. An aqueous solution of the salt (1 in 20) is neutral to litmus. When exposed to warm air, the salt loses some of its water of crystallization and is converted into a white powder. Further heating removes more water, and above 200° C. it is rendered anhydrous. An aqueous solution of the salt (1 in 20), when mixed with ammonium chloride T. S. and ammonia water, yields with sodium phosphate T. S. a white, crystalline precipitate. Another portion of the solution yields with barium chloride T. S. a white precipitate insoluble in hydrochloric acid. Add a few drops of silver nitrate T. S. to 10 mils. of an aqueous solution of the salt (1 in 20), previously mixed with a few drops of nitric acid; not more than an opalescence is produced (chloride). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part II, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part II, Test No. 1). (Official description.)

Dissolve about 1 Gm. of Magnesium Sulphate, accurately weighed, in 100 mils. of distilled water, gradually add to the solution, with constant stirring, an excess of sodium phosphate T. S. (about 20 mils.), allow to stand for 10 minutes, then add 30 mils. of ammonia water and allow to stand for two hours. Collect the precipitate on a filter, wash it with dilute ammonia water (1 volume of ammonia water to 3 volumes of distilled water) until 10 mils. of the washings, when acidulated with hydrochloric acid, yields no turbidity on the addition of a few drops of barium chloride T. S. Dry and ignite to constant weight. The weight of the magnesium pyrophosphate so obtained corresponds to not less than 48.59 per cent. nor more than 53.45 per cent. of $MgSO_4$. (Assay.)

CANTHARIS. (Official Latin name.)

CANTHARIDES. (Official English name.)

Canthar. (Official abbreviation.) Spanish Flies, Russian Flies (Synonyms.)

The dried beetle, *Cantharis vesicatoria* (Linné) De Geer (Fam. *Meloidæ*, Order *Coleoptera*), yielding not less than 0.6 per cent. of cantharidin. (Official definition.)

From 15 to 25 mm. in length, 5 to 8 mm. in breadth, oblong, somewhat compressed above; of a brilliant green or bluish-green, metallic lustre, changing in different parts, especially beneath, to a golden-green; head triangular, separated into two lateral lobes by a faint median line; mandibles stout and partly concealed; antennæ filiform, of 11 conical joints, the upper ones being black; eyes comparatively small; prothorax angulate; legs with five tarsal joints; wings membranous and brownish; elytra or wing sheaths each with two parallel lines and finely wrinkled; odor strong, disagreeable; taste slight, afterwards acrid. (Official description.)

Cantharides with an ammoniacal odor must not be used.

The powder is grayish-brown, with shining green particles and a number of long, pointed, 1-celled hairs 0.5 mm. in length and 0.020 mm. in width.

Cantharides does not contain more than 10 per cent. of moisture.

The yield of ash does not exceed 9 per cent.

Introduce 15 Gms. of Cantharides in No. 40 powder into a stout bottle of not less than 250 mils. capacity add 150 mils. of a mixture of benzene, two volumes, and purified petroleum benzin, one volume, and then add 2 mils. of hydrochloric acid. Stopper the bottle tightly, shake it well, and allow it to stand over night. Now gradually warm the bottle and its contents to about 40° C. and maintain it at that temperature with frequent shaking during three hours. Cool the mixture, decant or filter off 100 mils. of clear solution and evaporate this rapidly in a tared beaker or wide-necked flask to a volume of about 5 mils. Now add 5 mils. of chloroform to the residue and set it aside in a moderately warm place. When the solvent has all evaporated, add to the crystals 10 mils. of a mixture of equal volumes of dehydrated alcohol and purified petroleum benzin, which has previously been saturated with pure cantharidin, allow the mixture to stand securely covered, during fifteen minutes and then decant it through a pellet of purified cotton. Wash the crystals with successive portions of a saturated solution of cantharidin, similar to that directed above, until it is free from fat and coloring matter, and pass the washings through the same pellet of purified cotton. Then wash the cotton with a very small quantity of warm chloroform to dissolve any adhering crystals, collect the chloroform in the tared flask or beaker containing the washed crystals, evaporate off the solution with the aid of a blast of air, dry them at 60° C. for one-half hour and weigh. The resulting weight will be the amount of cantharidin obtained from 10 grammes of Cantharides. (Assay.)

The **official Latin name**, which very properly is given in the Latin language, owing to its security against change, is intended to be at once simple and distinctive, and must be accepted as representing the drug or preparation more particularly defined in the other subdivisions. In some instances the names by which drugs have been long known have been retained without any special reference to the

source, thus *Galla, Buchu, Opium, Senna, Kino, Sabal,* etc.; but in the majority of cases the generic or specific name of the plant or animal yielding the drug has been adopted as the official name, thus, *Aconitum, Althæa, Camphora, Arnica, Ipecacuanha, Coccus, Hyoscyamus, Moschus, Rheum, Senega,* etc. In order to avoid confusion a few of the former generic or specific names of plants have been retained as the official names of drugs now known to be derived from a different source, as in the case of *Asafœtida* from *Ferula fœtida, Cambogia* from *Garcinia Hanburii,* etc.

When different species of the same genus furnish different drugs it becomes necessary either to employ the full botanical name of the plants to distinguish the official varieties, or to select the generic name only for one of the drugs and a qualified name for others. Thus, the Pharmacopœia has chosen the generic name *Cinchona* to designate the barks of *Cinchona Ledgeriana* and *Cinchona Calisaya,* and of hybrids of these with other species, which are usually designated as Calisaya or Yellow Bark, and the name *Cinchona rubra* as the official title of the bark of *Cinchona succirubra* and its hybrids, commonly termed Red Bark.

Whenever different parts of the same plant are officially recognized as distinct drugs, the name of the particular part must be added to the generic or specific name of the plant, thus *Belladonnæ Folia,* and *Belladonnæ Radix, Colchici Cormus* and *Colchici Semen,* etc.

In the official names of compound preparations the principal constituents are as a rule specified, as *Liquor Ferri et Ammonii Acetatis, Pulvis Ipecacuanhæ et Opii;* but usage has sanctioned a modification of this rule when there are many ingredients, by naming one of them with the addition of an adjective, such as *compositus, a, um* (compound) *aromaticus, a, um* (aromatic), etc., thus making a simple comprehensive title, as *Spiritus Ammoniæ Aromaticus, Tinctura Cinchonæ Composita, Pilulæ Catharticæ Compositæ, Tinctura Opii Camphorata, Syrupus Rhei Aromaticus, Pulvis Jalapæ Compositus,* etc.

In the case of chemical compounds where similar combinations of the same elements, or several varieties of the same compound, have received recognition, it is absolutely necessary that the official name include some qualifying term by means of which the character of the substance may at once be recognized, thus *Hydrargyri Chloridum —Corrosivum* and *Mite, Hydrargyri Iodidum—Flavum* and *Rubrum, Ferri Sulphas—Exsiccatus* and *Granulatus,* etc.

The Latin official names are generally used in the singular number, even though the idea of plurality may be essentially connected with the drug, as in the case of Caryophyllus, Galla, Amygdala, etc.; this is in accordance with the precedent set by the Roman medical writers. Whenever a part of the plant also appears in the official name the following rule prevails: *Semen* (seed), *Cortex* (bark), and *Radix* (root) are always used in the singular, while *Folia* (leaves) and *Flores* (flowers) are invariably used in the plural.

The **official English name** need not necessarily be a literal translation of the official Latin name; in fact, it seems very desirable that a drug should have two distinct names officially recognized, that one confined to the official Latin title, admirably adapted to abbreviation and use in prescriptions, while the other may be employed in the ordinary course of conversation, and is intended for use in commercial transactions and the daily routine of business, as *Red Rose* for *Rosa Gallica*, *Wild Cherry* for *Prunus Virginiana*, etc. Occasionally the English name is used in the plural, while the Latin name is always used in the singular number, as *Cantharides* for *Cantharis*. In the case of chemical compounds the official English name often indicates with greater precision the true composition, as *Ferrous Sulphate* for *Ferri Sulphas*, *Ferric Chloride* for *Ferri Chloridum*, etc.

Immediately following the English name occurs the official abbreviation of the Latin name, introduced for convenience in prescription writing and in labeling containers of drugs, thus: *Fldext. Aconit.* for *Fluidextractum Aconiti*, *Lin. Calc.* for *Linimentum Calcis*, *Pot. Acet.* for *Potassii Acetas*, *Pil. Cathart. Co.* for *Pilulæ Catharticæ Compositæ*, etc. In the same line with the abbreviations, but in lighter face type, are given the official synonyms, which have been introduced partly for commercial purposes, but chiefly to insure conformity to the requirements of the Federal and State Food and Drug Laws, when drugs are imported or sold under names other than the official English name, thus: *Camphorated Oil* for *Liniment of Camphor*, *Bitter Apple* for *Colocynth*, *Calomel* for *Mild Mercurous Chloride*, *Epsom Salt* for *Magnesium Sulphate*, *Salol* for *Phenyl Salicylate*, *Golden Seal* for *Hydrastis*, *Spanish Flies* for *Cantharides*, *Dandelion* for *Taraxacum*, *White Precipitate* for *Ammoniated Mercury*, *German Chamomile* for *Matricaria*, *Henbane* for *Hyoscyamus*, *Labarraque's Solution* for *Solution of Chlorinated Soda*, *Extract of Witch Hazel* for *Hamamelis Water*, *Glauber Salt* for *Sodium Sulphate*, *Goulard's Extract* for *Solution of Lead Subacetate*, *Red Precipitate* for *Red Mercuric Oxide*, *Blaud's Pills* for *Pills of Ferrous Carbonate*, *Citrine Ointment* for *Ointment of Mercuric Nitrate*, *Monsel's Solution* for *Solution of Ferric Subsulphate*, *Yellow Cinchona* and *Yellow Peruvian Bark* for *Cinchona*, etc. The origin of these synonyms is not in strict accord with systematic nomenclature and often unscientific, but they serve a very useful purpose and are largely used by the public.

Official Definition.—The official definition determines the source and character of the drug or chemical as recognized by the Pharmacopœia. In the case of vegetable drugs the botanical name of the plant yielding the drug is composed of two parts, the generic name and the specific name, always written in the same order of sequence; the first or generic name is invariably begun with a capital letter, and is usually employed as the official Latin name of the drug, while the specific name is only begun with a capital letter when derived from a generic name, as in *Aconitum Napellus* and *Punica Granatum*, or from a

proper name, as in *Garcinia Hanburii*, or when it is indeclinable, as in *Theobroma Cacao*. The necessity for using the full botanical name of the plant to indicate the source of the official drug is clearly shown in the case of the genus *Lobelia*, of which the Pharmacopœia recognizes only the species *inflata*, although two others, *syphilitica* and *cardinalis*, are also well known; of the genus *Grindelia*, three species, *G. camporum*, *G. cuneifolia* and *G. squarrosa*, are recognized as furnishing the official drug. Accompanying the botanical name of the plant is the name of the author, printed in Roman type; and following it, enclosed in parentheses, the family to which the plant belongs—thus, *Rheum palmatum* Linné (Fam. *Polygonaceæ*).

In the case of chemicals, the official definition is expressed in three different ways: (1) A statement of the true character of the substance, more specifically indicated by a symbolic formula. (2) A statement of the character of the chemical, accompanied by the official purity requirement. (3) A simple statement of the official requirement of purity percentage. The official purity requirement is a most important statement, since the Pharmacopœia has been designated as a standard in the examination of drugs by the Federal and State Governments.

The following examples will serve to illustrate the three methods of expressing the official definition:

1. Under Acetanilid.—The monacetyl derivative [C_8H_7NO or $C_6H_5NH(CH_3CO)$] of aniline.

Under Morphine.—An alkaloid, ($C_{17}H_{19}NO_3 + H_2O$) obtained from opium.

2. Under Citric Acid.—A tribasic organic acid obtained from the juice of limes and lemons, and containing not less than 99.6 per cent. of $H_3C_6H_5O_7 + H_2O$.

Under Benzoic Acid.—An organic acid obtained from benzoin or prepared synthetically, and containing when dried to constant weight in a desiccator over sulphuric acid, not less than 99.5 per cent. of $HC_7H_5O_2$.

3. Under Ammonium Chloride.—It contains, when dried to constant weight at 100° C., not less than 99.5 per cent. of NH_4Cl.

Under Potassium Hydroxide.—It contains not less than 85 per cent. of KOH.

Symbolic formulas always express the exact composition of the chemicals which they represent, and must be assumed to indicate absolute purity.

Whenever water is expressed in a symbolic formula, as in the two cases above mentioned, it forms an integral part of that formula, and is shown to be an essential constituent of the official compound; in the majority of cases the presence of such water lends to the compound its power to assume the crystalline form, and is then known as water of crystallization, but when not so required it is known as water of hydration. Every symbolic formula is followed by a number which expresses the molecular weight of the compound—that is, the sum

of the weights of the atoms of component elements; thus in the case of the official sodium carbonate $Na_2CO_3 + H_2O = 124.02$, the molecular weight 124.02 is equal to the sum of the weights of all the atoms represented in the compound, namely, 2 atoms of sodium = (23 × 2) 46, 1 atom of carbon = 12, 3 atoms of oxygen = (16 × 3) 48, 2 atoms of hydrogen = (1.008 × 2) 2.016, 1 atom of oxygen = 16, or 46 + 12 + 48 + 2.016 + 16 = 124.02. Potassium bicarbonate is given as $KHCO_3 = 100.11$, in which case the weight of all the atoms in the compound is accounted for as follows: 1 atom of potassium = 39.1, 1 atom of hydrogen = 1.008, 1 atom of carbon = 12, 3 atoms of oxygen = (16 × 3) 48, or 39.1 + 1.008 + 12 + 48 = 100.11. Official morphine sulphate is given as $(C_{17}H_{19}NO_3)_2\ H_2SO_4 + 5H_2O = 758.49$, the sum of the weights of all the atoms indicated being made up as follows: Twice 17 = 34 atoms of carbon = (12 × 34) 408, twice 19 = 38 atoms of hydrogen = (1.008 × 38) 38,304, twice 1 = 2 atoms of nitrogen = (14.01 × 2) 28.02, twice 3 = 6 atoms of oxygen = (16 × 6) 96, 2 atoms of hydrogen = 1.008 × 2) 2.016, 1 atom of sulphur = 32.07, 4 atoms of oxygen = (16 × 4) 64, 10 atoms of hydrogen = (1.008 × 10) 10.08, 5 atoms of oxygen = (16 × 5) 80, or 408 + 38.304 + 28.02 + 96 + 2.016 + 32.07 + 64 + 10.08 + 80 = 758.49.

The number following simple elements expresses only the weight of a single atom, as bromine, Br = 79.92, sulphur, S = 32.07, etc. Atomic and molecular weights are of value in the proper construction of equations for the purpose of demonstrating chemical reactions.

The Official Description.—While the official definition is a brief but exact statement of the nature and source of drugs and of the composition of chemicals, the official description amplifies the definition by adding the physical characteristics of drugs, such as shape, size, odor, and taste, together with a statement of possible impurities and adulterations, and means for their detection. For chemicals, are added a clear account of their physical properties, their behavior toward different solvents, and such tests as shall enable the pharmacist to detect impurities and establish the fulfilment of pharmacopœial requirements. The official description is always printed in small type, and forms a most valuable and important part of the Pharmacopœia.

In the case of many animal and vegetable drugs, an accurate description of the powdered drug is also given, and assay processes, or methods for determining the quality or purity percentage of official drugs, animal, chemical and vegetable, are appended wherever practicable.

DISPENSATORIES.

A dispensatory is a commentary on the Pharmacopœia, and, as such, has become indispensable to both physicians and pharmacists. While the text of the Pharmacopœia is confined to the definition and description of drugs and chemicals as well as to the official tests and requirements and accepted formulas for numerous preparations,

much valuable additional information is given in the dispensatories, such as historical data, action, and uses, as well as doses of medicines, together with comments on and explanations of pharmaceutical and chemical processes. Besides the official drugs and chemicals, a large number of unofficial remedies and formulas are also treated in detail. Three dispensatories are published in this country: the *United States Dispensatory*, established in 1833, by Wood and Bache, which is now edited by Wood, Remington, and Sadtler, and reached its twentieth edition in 1916; the *American Dispensatory*, first edited by John King, M.D., in 1854, of which the eighteenth edition, entirely rewritten by Lloyd and Felter, was issued in two volumes in 1898 and 1900; and the *National Dispensatory*, established in 1879 by Stillé and Maisch, of which five editions were published, and which, after the death of the original authors, was superseded by the *National Standard Dispensatory*, edited by Hare, Caspari, and Rusby, the third edition of which was issued in 1916.

THE NATIONAL FORMULARY.

The *National Formulary* originated with the American Pharmaceutical Association, and was first published in 1886. It is a book of formulas and directions for making a large number of pharmaceutical preparations not found in the Pharmacopœia, and, like the latter authority, has received official recognition by Congress as a standard in the enforcement of the Pure Food and Drugs Act of 1906. Thus far three revised editions of the *National Formulary* have appeared, the last in 1916.

CHAPTER II.

WEIGHTS AND MEASURES.

Metrology.—Metrology (from the Greek μέτρον, measure, and λόγος, a discourse) is a study of the art and science of measurements as applied to extension, volume, and weight of matter. Measure of extension may be either of length or of surface, while measure of volume or bulk applies to the cubic contents. Measure of weight is the determination of the gravitating force of bodies—that is, of their attraction by the earth toward its centre, such attraction bearing a direct relation to the quantity of matter contained in a body; hence weight is pressure exerted by a body upon a horizontal plane supporting it; and the operation of weighing may be defined as the process of determining the number of standard masses (grammes, grains, ounces, or pounds, as the case may be) which are attracted by the earth with as much force as is the body that is being weighed. True weight can be obtained only *in vacuo*, where the exact measurements of the force of gravitation cannot be interfered with by atmospheric pressure; all measurements of weight in any medium, such as air or water, must therefore give low results. Ordinary operations of weighing, being conducted in air, give apparent weight of the substance only.

Weighing and measuring being operations of daily occurrence in pharmacy which require care and exactness, a knowledge of the standards of weights and measures in use in this country and elsewhere is absolutely necessary. With more or less modification the standards at present in use in pharmacy in the United States and Great Britain are the same as those formerly employed by the Romans, and which in all probability were derived by them from the more ancient Greek nation. Three different systems of weights are at present employed by all English-speaking nations, namely, avoirdupois weight, apothecaries' weight and metric weight.

Avoirdupois Weight.—Avoirdupois weight, as its name would seem to indicate, is probably of French origin (*avoir du poids*, to have weight), and was no doubt introduced into Great Britain during the reign of the Norman dynasty; it first appeared in the English statute-books in 1335 and is now designated Imperial weight throughout the British Empire. Avoirdupois weight is employed in the sale of all commodities except precious metals and precious stones; hence drugs are always bought and sold by pharmacists by this system. In 1824 the value of an avoirdupois pound was defined by law in England to be $\frac{7000}{5760}$ of the standard troy pound. The divisions of avoirdupois weight are the

pound, ounce, drachm, and grain, which are symbolized by the following characters: lb., oz., drm., gr.; each pound contains 16 ounces and each ounce 16 drachms or 437½ grains. The term drachm is rarely employed, quantities less than an ounce being usually designated by common fractions, such as $\frac{1}{16}$ oz., $\frac{1}{8}$ oz., $\frac{1}{4}$ oz., or in grains. The avoirdupois pound containing 7000 grains ($437\frac{1}{2} \times 16$) is the only pound used in the United States and Great Britain except at the mints; the standard pound is the equivalent in weight of 27.7274 cubic inches of distilled water at 62° Fahrenheit and normal barometric pressure.

Apothecaries' Weight.—Apothecaries' weight was probably derived from troy weight, which latter was introduced into Great Britain, by merchants from Lombardy, toward the close of the thirteenth century; it is employed altogether in the writing and compounding of physicians' prescriptions, and is divided into grains, scruples, drachms, and ounces, of which 20 grains are equal to 1 scruple, 3 scruples are equal to 1 drachm, and 8 drachms are equal to 1 ounce. The apothecaries' ounce is of the same value as the now obsolete English troy ounce. The following symbols are employed to designate the divisions of apothecaries' weight, and always precede the number indicating the quantity intended, which is expressed in Roman numerals; thus, gr. j, for one grain; ℈ij, for two scruples; ʒiij, for three drachms; ℥iv, for four ounces. As far back as 1266, during the reign of Henry III, a statute was enacted in England, which provided that an English silver penny, called a sterling, round and without clipping, should equal in weight 32 wheat-grains, well dried and taken from the centre of the ear, and that of such pence 20 should make 1 ounce, and 12 ounces 1 pound. About 1497, in the time of Henry VII., the weight of the silver penny, however, was changed to the equivalent of 24 wheat-grains. These statutes clearly indicate the origin of the pennyweight and the troy system, from which the apothecaries' weight, still in use at the present day, was subsequently derived. The choice of wheat-grains from *the centre of the ear* arose from a desire for uniformity in size and weight, as did likewise the directions to employ the grain *well dried*. The adoption of troy weight by physicians and pharmacists dates back to 1618, when the first London Pharmacopœia was compiled. In 1826 Imperial measures and standards were legalized in England, and in 1827 exact copies of these standards were furnished the minister of the United States Government at London, namely, the standard yard, a bronze bar of 36 inches length, a brass troy-pound weight of 5760 grains, and a brass avoirdupois-pound weight of 7000 grains; copies of these standards were supplied to the different States in 1836 by act of Congress. These standards remained in use until 1893, when the United States Government authorized a change so as to bring the yard and pound into direct relation to the metric standards adopted by the International Bureau of Weights and Measures at Paris, which latter was established and is maintained jointly by the principal governments of the world.

From what has been said above it is clear that every apothecaries' ounce is heavier than the avoirdupois ounce by 42½ grains; hence to find the corresponding value in avoirdupois ounces of any given number of apothecaries' ounces, add to the latter $\frac{42\frac{1}{2}}{437\frac{1}{2}} = \frac{85}{875}$ or $\left(\frac{17}{175}\right)$ of that number; thus ℥xxiv = 24 avoirdupois ounces plus $\frac{17}{175}$ of 24, which is 24 + 2.33, or 26.33 ounces; or multiply the number of apothecaries' ounces by 480 and divide the product by 437.5, the quotient representing the corresponding avoirdupois weight in ounces. If, on the other hand, avoirdupois weight is to be converted into apothecaries' weight, subtract from the number of ounces given $\frac{42\frac{1}{2}}{480} = \left(\frac{85}{960} \text{ or } \frac{17}{192}\right)$ of the number; thus 26.33 ounces = $26.33 - \frac{17}{192}$ of 26.33, which is equal to 26.33—2.33, or 24 apothecaries' ounces; or multiply the number of avoirdupois ounces by 437.5 and divide the product by 480, the quotient representing the corresponding apothecaries' weight in ounces.

While apothecaries' weight is employed in compounding prescriptions both in this country and Great Britain, it is not used in either the United States or the British Pharmacopœia, and will no doubt be entirely abolished in the course of time, when a uniform international system of weights shall have been adopted by the medical and pharmaceutical professions of both countries. The grain is the connecting link between avoirdupois, troy, apothecaries', and Imperial weight, being the same in all.

Fluid Measure.—The fluid measure used by pharmacists of the United States is derived from the old wine measure of England (now extinct), which allowed to each wine gallon the volume of 231 cubic inches, or 58340.011 grains of distilled water at 15° C. (59° F.); the Imperial gallon of Great Britain contains 277.274 cubic inches, or 70,000 grains of distilled water at 62° Fahr. In both cases the gallon is divided into 8 pints; but the pint of wine measure contains 16 fluidounces, while the Imperial pint contains 20 fluidounces. The United States fluid measure has the following units: the minim, the fluidrachm, and the fluidounce, which are represented by the following signs: ♏, f℥, f℥; in addition, the pint and gallon are sometimes employed in commercial transactions, being designated by the abbreviations, *O*, from *Octarius*, for pint, and *Cong.*, from *Congius*, for gallon. The units of Imperial fluid measure bear the same names as those employed for United States fluid measure, but differ from them in value; thus, while the Imperial minim of water weighs 0.91 (0.9114583) grain, the United States minim of water weighs 0.95 (0.9493) grain, and, since both fluidounces contain 480 minims, the Imperial fluidounce of water weighs 437.5 grains, but the United States fluidounce 455.70 grains, at 15.6° C. (60° F.). Each fluidounce is divided into 8 fluidrachms and each fluidrachm into 60 minims.

It must not be overlooked that many liquids, although dispensed and sold by the apothecary by fluid measure, are purchased from the manufacturer by weight, and whenever the specific gravity of the liquid differs materially from that of water there must be also a marked difference in the relative volume; thus glycerin, syrups, chloroform, ethers, acids, essential oils, and many chemical solutions are always purchased by weight. The following list shows the number of fluidounces in one pound of the respective liquids, of pharmacopœial quality:

One pound of	Sulphuric Acid measures about	8⅓	fluidounces.
" "	Monsel's Solution measures about	10	"
" "	Chloroform " "	10⅓	"
" "	Syrup " "	11⅓	"
" "	Glycerin " "	12⅓	"
" "	Goulard's Extract " "	12⅔	"
" "	Ammonia Water " "	16	"
" "	Stronger Ammonia Water measures about	17	"
" "	Spirit of Nitrous Ether "	18⅓	"
" "	Essential Oil measures from	13 to 18	"
" "	Ether measures about	21⅓	"

The Metric or Decimal System.—The metric or decimal system of weights and measures, which is the only official system of the present United States Pharmacopœia, is supposed to have originated in the fertile mind of the French statesman, Prince de Talleyrand, toward the close of the eighteenth century, and was enforced in France by law in December, 1799. It has already become the legal standard in all civilized countries except the United States and Great Britain, and is destined to become the universal standard for commercial transactions, as it is already for strictly scientific work, the world over.

The use of metric weights and measures was legalized in the United States and Great Britain in 1866, but neither country has as yet officially adopted them, although the prospects for such desirable action are brightening. In 1878 the use of the metric system of weights and measures was made obligatory in the medical department of the United States Navy, and in 1894 in the medical department of the United States Army; in 1902 it was ordered that for all official, medical, and pharmacal purposes in the United States Public Health and Marine Hospital Service metric weights and measures only shall be employed. For some years past efforts have been made annually by the American Pharmaceutical Association to induce Congress to pass laws looking to the introduction of the metric system of weights and measures in place of those now in use, but thus far without success. Since the introduction of a new system of weights and measures must, no doubt, for a time create some confusion, a careful study of the same is required of pharmacists and physicians. The principles upon which the metric system was founded are as follows: The reduction of all weights and measures to one uniform standard of linear meaures; the use of an aliquot part of the earth's circumference as such standard; the application of the unit of linear measure to matter in its three

modes of extension—length, breadth, and thickness—as a standard of all measures of length, surface, and solidity; the cubic contents of linear measure in distilled water at the temperature of its greatest density to furnish at once the standard measure of weight and of capacity; everything susceptible of being weighed or measured to have only one measure of weight, one measure of length, and one measure of capacity, with their multiples and subdivisions exclusively in decimal proportions; and every weight and every measure to be designated by an appropriate significant characteristic name applied exclusively to itself.

As a basis, the authors of the metric system adopted a quadrant (one-fourth) of the earth's circumference, and dividing this into ten million parts they obtained a certain measure of length, which they named METER (French *mètre*) and adopted as a standard for all units of measurements; this meter, which was made the unit of linear measure, is equal to 39.3704 inches. One-tenth part of the meter, applied to cubic measurement, was made the unit of measure of capacity and called a LITER (French *litre*); it is equal to 33.8149 U. S. fluidounces or 2.1135 wine pints. The one-thousandth part of the liter (which is equal to the cube of one-hundredth part of the meter) was chosen to furnish the unit of weight; the weight of such a volume of distilled water at its greatest density, 4° C. (39.2° F.), was called a GRAMME. and is equal to 15.43235639 grains. The multiples of these units are denoted by prefixes of the Greek numerals, *deka* 10, *hecto* 100, *kilo* 1000, *myria* 10,000; while prefixes of the Latin numerals denote the subdivisions, thus *deci*, one-tenth; *centi*, one-hundredth, and *milli*, one-thousandth A special subdivision of the meter has been adopted by scientists for use in microscopic measurements; it is the micromillimeter or micron, and represents the thousandth part of a millimeter. It is equivalent to about $\frac{1}{25000}$ of an inch, and is expressed by the symbol μ; the double symbol $\mu\ \mu$ is used to indicate the thousandth part of a micron. Although the liter is the unit of measures of capacity, the subdivisions of this unit are almost invariably spoken of as so many milliliters (or cubic centimeters), since each liter is equal to 1000 milliliters (or cubic centimeters); thus the expressions 10, 50, 100, 250, 750 milliliters (or cubic centimeters), etc., are preferred to 1 centiliter, 5 centiliters, 1 deciliter, one-fourth of a liter, and three-fourths of a liter. In like manner the specific names of the fourth multiple of the units are rarely employed, it being customary to designate all above the third multiple as so many of that multiple; thus 10 kilometers instead of 1 myriameter, 15,000 liters instead of 1½ myrialiter, and 20 kilograms instead of 2 myriagrams, etc.

The original metric standards were made of platinum by Borda, of Paris, and were designated respectively "le metre des archives" and "le kilogramme des archives." The actual standards now in use are made of an alloy composed of platinum 90 per cent. and

iridium 10 per cent by the International Bureau of Metric Weights. and Measures; copies of these standards have been furnished to all civilized nations, those intended for the United States having been received by our Government in 1890. The theoretical units are not identical with the actual standards now in use. Thus, the theoretical meter is one ten-millionth part of the quadrant, while the actual meter is the standard meter of the International Metric Bureau; likewise the theoretical liter is the cubic decimeter, while the actual liter is the volume at 4° C. of one actual kilogram of water, and is equivalent in volume to 1.000027 cubic decimeters or 1000.027 cubic centimeters. The theoretical kilogram is the mass or quantity of one cubic decimeter of water at 4° C., while the actual kilogram is the mass or quantity of the standard kilogram of iridio-platinum of the International Metric Bureau.

When writing the names of metric measures and weights, abbreviations are usually employed in place of the full names, as will be seen from the following tables, which also give the corresponding values in customary weights and measures:

Measures of Length.

1 Myriameter,	Mm.	= 10000.0	M	= 6.2137 +	miles.
1 Kilometer,	Km.	= 1000.0	"	= 4.9710 +	furlongs.
1 Hectometer,	Hm.	= 100.0	"	= 19.8840 +	rods.
1 Dekameter,	Dm.	= 10.0	"	= 32.8086 +	feet.
1 Meter,	M.	= 1.0	"	= 39.3704	inches.
1 Decimeter,	dm.	= 0.1	"	= 3.93704	"
1 Centimeter,	cm.	= 0.01	"	= 0.393704	inch.
1 Millimeter,	mm.	= 0.001	"	= 0.0393704	"

Measures of Capacity.

1 Myrialiter,	Ml.	= 10000.0	L.	= 2641.7890 +	gallons.
1 Kiloliter,	Kl.	= 1000.0	"	= 264.1789 +	"
1 Hectoliter,	Hl.	= 100.0	"	= 26.4178 +	"
1 Dekaliter,	Dl.	= 10.0	"	= 2.6417 +	"
1 Liter,	L.	= 1.0	"	= 33.8149 +	fluidounces.
1 Deciliter,	dl.	= 0.1	"	= 3.38149 +	"
1 Centiliter,	cl.	= 0.01	"	= 0.338149 +	fluidounce.
1 Milliliter,	ml.	= 0.001	"	= 0.0338149 +	"
1 Cubic centimeter,	ccm.	= 0.001	"	= 0.0338149 +	"

Measures of Weight.

1 Myriagram,	Mg.	= 10000.0	Gm.	= 22.0461 +	pounds.
1 Kilogram,	Kg.	= 1000.0	"	= 2.2046 +	"
1 Hectogram,	Hg.	= 100.0	"	= 3.5273 +	av. ozs.
1 Dekagram,	Dg.	= 10.0	"	= 154.3235639	grains.
1 Gram,	Gm.	= 1.0	"	= 15.43235639	"
1 Decigram,	dg.	= 0.1	"	= 1.543235639	"
1 Centigram,	cg.	= 0.01	"	= 0.1543235639	grain.
1 Milligram,	mg.	= 0.001	"	= 0.01543235639	"

The U. S. Pharmacopœia has introduced the word "mil" to be used as a short form or contraction for milliliter, in place of the abbreviation "ml."[1] The numerical expression of all weights, and measures should

[1] Throughout this book the abbreviation or contraction of milliliter will be written as follows: mil. for the singular and mils. for the plural of milliliter.

always be accompanied by the abbreviation used for the unit, and whenever subdivisions are not given a cipher should follow the decimal point, so as to indicate more clearly the intention of the writer; thus, 25.0 Gms. and 350.0 mils. (or Cc.), leave no doubt whatever as to the quantities desired, whereas 25 Gms. and 350 mils. (or Cc.) might have been carelessly written for 2.5 Gms. and 35.0 mils. (or Cc.). Since the value of the numerical expression depends entirely upon the correct placing of the decimal point, due care must be observed lest the misplacement thereof increase or decrease the intended value tenfold. When reading metric weights and measures the multiples of the units should be read as so many units, but the subdivisions are preferably named as so many of the lowest division possible; for instance, 25.050 Gms. should be read 25 grams and 50 milligrams instead of 25 and $\frac{5}{100}$ grams; 0.125 Gm., 125 milligrams instead of 12½ centigrams or 1 decigram 2 centigrams and 5 milligrams; 0.020 M. should be read as 2 centimeters or 20 millimeters, but never as $\frac{2}{100}$ or $\frac{20}{1000}$ of a meter; 1.425 L. should be read as 1425 milliliters or cubic centimeters instead of $1\frac{425}{1000}$ liter or 1 liter and 425 milliliters or cubic centimeters.

Since the milliliter, or the one-thousandth part of the actual liter now in use, is slightly larger than the cubic centimeter (1.000027), the U. S. Bureau of Standards at Washington has abolished the latter name for the lowest subdivision of metric liquid measure, as have also the U. S. and British Pharmacopœias, but scientists will no doubt continue to use it, at least as long as burettes, cylinders, flasks and other apparatus continue to be graduated in cubic centimeters. The difference between a milliliter and a cubic centimeter is but trifling, and for all practical purposes the two names represent identical measures of capacity.[1]

The following table of comparison between customary and metric weights and measures will be found convenient for reference, and should be carefully studied in order that the relative values may become gradually fixed in the mind:

1 kilometer = 0.62137 (nearly ⅝) of a mile.
1 meter = 39.37 (practically 39¼) inches, or 3.281 feet, or 1.0936 yards.
1 centimeter = 0.3937 (practically ⅜) of an inch.
1 millimeter = 0.03937 (practically $\frac{1}{25}$) of an inch.
1 mile = 1.6093 kilometers.
1 yard = 0.9144 meter.
1 foot = 0.3048 meter, or 30.48 centimeters.
1 inch = 2.54 centimeters, or 25.401 millimeters.
1 hectare = 2.471 acres.
1 acre = 0.4047 hectare.
1 square meter = 1.196 square yards, or 10.764 square feet.
1 square centimeter = 0.155 (practically ⅙) of a square inch.
1 square millimeter = 0.00155 (practically $\frac{1}{650}$) of a square inch.
1 square yard = 0.8361 square meter.

[1] For the convenience of students, the author has decided to place (cubic centimeter, or its abbreviation Cc.) immediately after the word milliliter, or its abbreviations mil. and mils., wherever the latter occur in this book.

1 square foot = 929.0341 square centimeters.
1 square inch = 645.16 square millimeters, or 6.4516+ square centimeters.
1 liter = 1.057 liquid quarts, or 0.9081 dry quart or 2.113+ pints, or 33.815 fluidounces.
1 milliliter (also designated by many 1 cubic centimeter) = 16.23 minims.
1 U. S. gallon = 3.7854 liters.
1 U. S. dry quart = 1.1012 liters.
1 U. S. liquid quart = 0.946 liter.
1 U. S. pint = 473.167 milliliters (or cubic centimeters).
1 U. S. fluidounce = 29.57+ (practically 30) milliliters (or cubic centimeters).
1 U. S. fluidrachm = 3.6967 (nearly 4) milliliters (or cubic centimeters).
1 kilogram (usually abbreviated 1 kilo) = 2.2046 (practically 2⅕) pounds avoirdupois.
1 gram = 15.4234 grains.
1 milligram = 0.01543 (practically $\frac{1}{64}$) grain.
1 pound (avoirdupois) = 453.6 grams.
1 pound (troy) = 373.24 grams.
1 ounce (avoirdupois) = 28.35 grams.
1 ounce (apothecaries' or troy) = 31.103 grams.
1 drachm (apothecaries') = 3.8879 (practically 4) grams.
1 scruple (apothecaries') = 1.2959 grams.
1 grain = 0.0648 gram, or 64.8 (nearly 65) milligrams.

The following simple rules will enable anyone readily to convert metric weights and measures into those customary in this country, the results being practically correct.

For linear measure: Divide the number of millimeters by 25, 300, or 900; the quotient will be the answer in inches, feet, or yards respectively.

For measures of capacity: Divide the number of milliliters (or cubic centimeters) by 0.06161, 3.697, or 29.57; the quotient will be the answer in U. S. minims, fluidrachms, or fluidounces, respectively.

For weight: Divide the number of grams by 0.06479, 3.8874, or 31.103; the quotient will be the answer in grains, drachms, or apothecaries' ounces, respectively. If the number of grams be divided by 28.35 or 453.6, the quotient will be the answer in ounces or pounds, avoirdupois weight, respectively.

In the actual operations of weighing and measuring, however, it will be found more desirable to be provided with a set of accurate metric weights and measures; for then even the slight errors arising from the translation of one system into another can be avoided.

COMPARATIVE TABLE OF METRIC WITH AVOIRDUPOIS AND APOTHECARIES' WEIGHTS.

Names.	Numerical Expressions.	Equivalents in Grains.	Equivalents in Avoirdupois Weight.			Equivalents in Apothecaries' Weight.		
	Gm.	Gr.	lb.	oz.	gr.	℥	ʒ	gr.
Milligram	0.001	0.01543	...	...	$\frac{1}{64}$	...	...	$\frac{1}{64}$
Centigram	0.010	0.15432	...	...	$\frac{1}{6}$	...	...	$\frac{1}{6}$
Decigram	0.100	1.54323	...	...	1.5	...	...	1.5
Gram	1.0	15.43235	...	...	15.4	...	...	15.4
Dekagram	10.0	154.32356	...	¼	45.0	...	2	34.0
Hectogram	100.0	1543.23563	...	3½	12.0	3	1	43.0
Kilogram	1000.0	15432.35639	2	3½	10.47	32	1	12.4
Myriagram	10000.0	154323.56390	22	½	14.8	321	4	3.5

In writing prescriptions, physicians are in the habit of considering 4 mils. (or Cc.) (actually 3.6969) as equivalent to 1 fluidrachm, and 30 mils. (or Cc.) (actually 29.573) as equivalent to 1 fluidounce.

COMPARATIVE TABLE OF METRIC AND APOTHECARIES' FLUID MEASURE.

Milliliter.	Minims.	f℥	f℥	♏
0.06161+	1.0	..	..	..
0.30805	5.0	..	..	..
0.61610	10.0	..	..	..
1.0	16.23+	..	..	..
5.0	81.15+	..	1	21.15
10.0	162.31	..	2	42.3
20.0	324.62	..	5	24.6
30.0	486.93	1	0	6.9
40.0	649.24	1	2	49.2
50.0	811.55	1	5	31.5
60.0	973.86	2	0	13.8
70.0	1136.17	2	2	56.1
80.0	1298.48	2	5	38.4
90.0	1460.79	3	0	20.7
100.0	1623.11	3	3	3.0
250.0	4057.77	8	3	37.5
500.0	8115.55	16	7	15.0
1000.0	16231.10	33	6	30.0

Physicians and pharmacists cannot be too careful in the use of metric weights and measures in the writing and reading of prescriptions. In continental Europe, where the metric system has been in use for many years, no signs are used in prescriptions, because all ingredients, whether solid or liquid, are weighed, and it is understood that weight is always intended; whenever, for any reason, measures are wanted, the signs L. (liter) and ccm. (cubic centimeter) are employed. But in this country, and also in England, where it is still, and likely to remain, customary to weigh solids and to measure fluids in the dispensing of medicines, the official abbreviations given in the U. S. Pharmacopœia should be used invariably, so as to avoid all possible confusion. With water, and the average diluted alcohol tinctures, it would probably not make much difference whether grammes or milliliters (cubic centimeters) were dispensed, but in the case of all liquids having a higher or lower specific gravity than water a marked variation will be observed; thus 20 Gms. of glycerin measure 16 mils. (Cc.) and 20 mils. (Cc.) of glycerin weigh 25 Gms.; 60 Gms. of simple syrup measure 45.5 mils. (Cc.), and 60 mils. (Cc.) of syrup weigh 79.02 Gms.; 30 Gms. of chloroform measure 20.13 + mils. (Cc.), and 30 mils. (Cc.) of chloroform weigh 44.7 Gms.; 4 Gms. of bromoform measure only 1.4 mils. (Cc.) and 4 mils. (Cc.) of bromoform weigh 11.32 Gms.; 10 Gms. of ether measure 13.77 + mils. (Cc.), and 10 mils. (Cc.) of ether weigh only 7.26 Gms.; 50 Gms. of alcohol measure 60.97 + mils. (Cc.), and 50 mils. (Cc.) of alcohol weigh 41 Gms.

It is incumbent upon the medical schools of this country to familiarize their students with the decimal system of weights and measures, as

is now done in all colleges of pharmacy; and not until the national medical and pharmaceutical associations shall have agreed upon some rule or guide for the two professions in the specification of metric weights and measures in prescriptions will the pharmacist be relieved of annoyance and censure caused by improper interpretation of quantities.

In the absence of specified fluid measures it is safest to follow the custom of continental Europe and weigh all solids and liquids when dispensing prescriptions written in the metric system.

The commercial weights and measures in use in this country are derived from the prototype standards furnished by the International Bureau of Weights and Measures, which are carefully preserved at the Bureau of Standards at Washington, D. C. Thus the yard is equal to 0.91440183 or $\frac{3600}{3937}$ of the meter, by which all foot rules and other long measure instruments are verified; the pound is equal to 0.4535924277 of the international kilogram, which latter in 1893 replaced the former old brass standard pound; the liquid gallon (wine gallon) is equivalent to the volume of 231 cubic inches, or 3.785332 liters.

The instruments used in weighing and measuring are balances, weights, and graduated vessels, and the necessity for their accuracy and careful preservation cannot be too strongly emphasized.

The Balance.—The balance or, as it is commonly called, "a pair of scales," is no doubt the most useful instrument in the hands of the pharmacist, for upon its proper construction and sensitiveness depend the accuracy of weighing and correct dispensing of medicines. The general construction of an ordinary balance is so well known that a detailed description seems unnecessary; the simple hand scales (see Fig. 1), which were formerly relied upon altogether, have almost completely disappeared in this country; in their stead a more substantial instrument is now used. The single beam principle still prevails in which a metallic bar is supported at its centre on a knife-edged axis, called the fulcrum, thus producing to arms of equal length. The fulcrum projects from the sides of the beam, and rests on two supports at the top of a stationary column, so constructed that the wear and tear due to constant friction is relieved by a special contrivance for raising the beam above the steel or agate plane when the balance is not in actual use. The knife-edged axis and the support on which it rests are both made of hardened steel and highly polished, in order to reduce friction to a minimum; but since even steel is liable to become rusty, particularly when exposed to moisture or acid vapors, agate edges and planes, which are practically indestructible, are now perferred on all finer balances. The center of gravity of the beam, which is the point through which the sum of the separate attractions of all the particles of the beam passes and operates as one force, should be located slightly below the edge of the fulcrum; if it were in the

edge of the fulcrum, the beam would not come to a horizontal position when the pans are equally loaded, but would remain in any position where it might chance to be placed. If it were above the edge of the fulcrum, the beam would remain horizontal if placed so; but if slightly deflected, it would tend to overturn by the action of the weight of the beam. The nearer the center of gravity comes to the edge of the fulcrum, the more accurate and sensitive will the balance be; but at the same time the beam will turn more slowly. The scale-pans are suspended in suitable wire frames, also supported by means of knife edges from the ends of the beam; in order to insure perfect equilibrium it is essential that the end knife edges be situated equally distant from the central point of support, and that they lie in the same plane

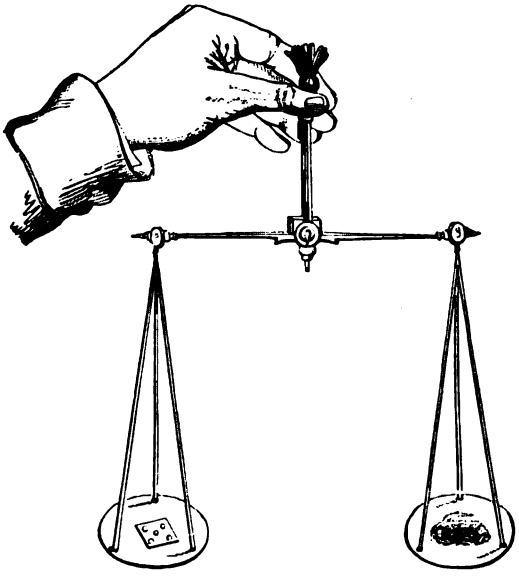


FIG. 1.—Old-style hand balance.

with it, all three edges being parallel to each other. The lighter in weight and the more inflexible the beam, the greater will be the sensitiveness of the balance. Both of these desirable qualities are obtained by the use of aluminum beams, which are also non-corrosive and non-magnetic.

The scale-pans are preferably made of solid nickel or solid silver; but for weighing certain chemical substances likely to attack the metal they should be supplanted by strong glass pans. Each balance is provided with an indicator in the form of a long, thin, flat needle attached to the centre of the beam, and so arranged that when the beam is in perfect stable equilibrium it points directly to the zero mark on a short graduated plate attached to the front base of the upright (see Fig. 2); on some balances the indicator points upward, the

graduated scale being placed at a little distance above the beam (see Fig. 3). When the balance is in use, it is far better to rely upon the regular, uniform oscillations of the beam, as shown by the indicator on the scale, than to await the fixed position of the indicator at the zero point. Every balance when purchased should be carefully tested as to its sensitiveness and correct adjustment; this is best done by allowing the beam to oscillate freely supported on its fulcrum, with the pans detached. The oscillations should be regular and the beam finally return to its horizontal position of rest; but it must be borne in mind that an essential requisite for the success of this test is a perfectly level position of the balance. The equilibrium of the beam should also be maintained when the pans are attached, whether empty or lightly or heavily loaded, and when the load is transposed from one pan to the other; these tests prove equality in the length of the arms.

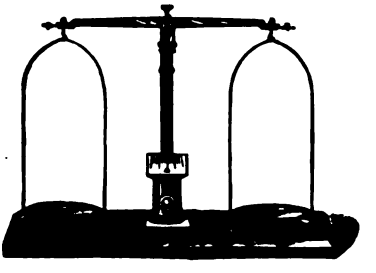


FIG. 2.—Prescription balance with indicator below the beam.

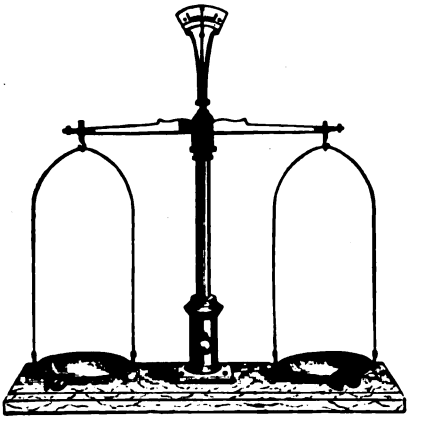


FIG. 3.—Prescription balance with indicator above the beam.

Prescription balances, sensitive to $\frac{1}{100}$ grain and intended only for weighing small quantities, whereby their accuracy can be maintained for a very long time, are offered of superior workmanship and provided with spirit level, levelling screws, and other devices to insure correctness in weighing (see Fig. 4). All fine balances should be kept enclosed in a suitable case provided with glass sides and top to protect them against dust, moisture, and corrosive vapors; they should not be scoured at any time, but simply polished with a piece of soft chamois skin or dusted with a soft camel-hair brush; under no circumstances should oil or chalk be used on the knife edges or planes.

Compound lever balances differ from those above described chiefly in having the pans situated above the beam and supported upon rods so constructed as to retain their vertical position during oscillation; they are less sensitive than the single beam prescription balances, and are generally used for coarser weighing. When enclosed in a box

they are known as "box scales," and then possess the advantage of having the more delicate parts of the mechanism protected against injury.

Figs. 5 and 6 show prescription and counter box scales constructed on the compound lever principle. Fig. 7 represents a convenient

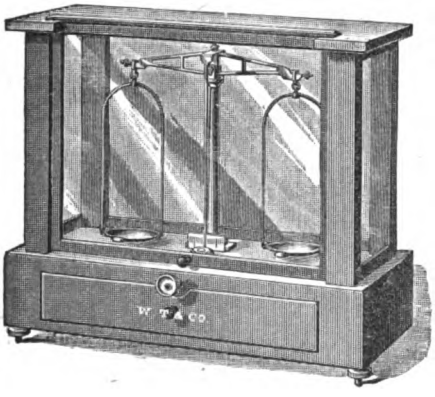


FIG. 4

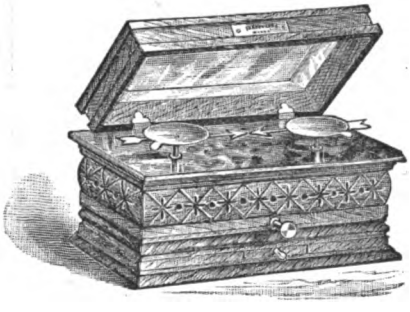


FIG. 5.—Prescription box scales.

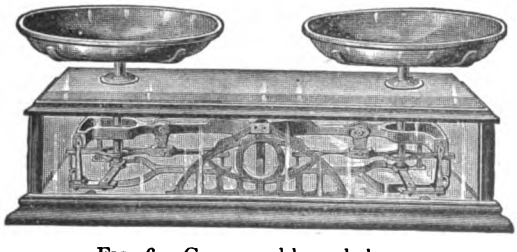


FIG. 6.—Compound lever balance.

dispensing balance for rough prescription work, and is intended for quantities ranging from 30 grains to 4 ounces; it is sensitive to ½ grain, and is provided with a beam graduated into apothecaries' and metric weight (1 to 120 grains and 0.1 to 8.0 Gm.) and carrying a sliding poise.

Special balances for weighing liquids, particularly in the laboratory, have been found very convenient on account of their peculiar construction. Fig. 8 represents Troemner's new solution balance, capable of weighing from 10 grams to 16 kilograms (154 grains to about 36 pounds). The scale is provided with an extra balancing beam, by which an empty bottle or container is quickly balanced by simply sliding the balance weight along until a correct balance is secured. A new system of adjusting weights, known as the ball system, is

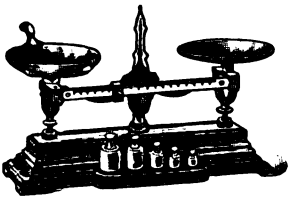


FIG. 7.—Troemner's dispensing scale.

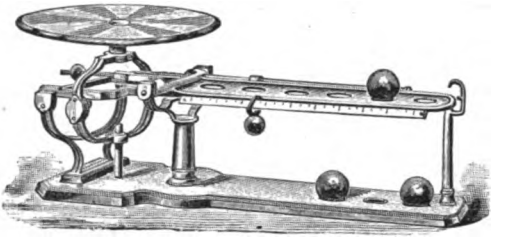


FIG. 8.—Troemner's new solution balance.

attached, and is a great improvement over the old method of using separate weights; small weights are adjusted on the graduated beam in front, while the larger weights are represented by different positions of the balls on the central plate.

Torsion Balances.—Although the principle underlying the construction of these balances was first applied by Profs. Gauss and Weber of the University of Göttingen, Germany, many years ago, their successful production is entirely due to the experimental work of Messrs. Roeder and Springer of Cincinnati, O., who, in 1882, overcame

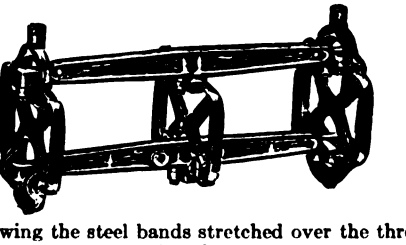


FIG. 9.—Showing the steel bands stretched over the three frames supporting the beam.

the difficulties of previous investigators. The chief difference between torsion and other balances lies in the entire absence of knife edges and the location of the center of gravity above the fulcrum or point of rotation. In torsion balances the knife edges have been replaced by thin steel bands or springs tightly stretched over the edges of the three frames supporting the beam (see Fig. 9). The center of the beam is fastened to the center of the strained band or spring and at right angles to it, under which condition, by the elasticity or torsion of the

band or spring it will vibrate exactly as the ordinary beam balanced on knife edges; the pans rest upon similar torsion bands or springs at the ends of the beam in the same manner as the central fulcrum of the beam. The name torsion balance is applied to these instruments on account of the slight twist given to the stretched bands or springs during oscillation of the beam, the term torsion being derived from the Latin verb *torquere* meaning to twist.

The first device to overcome the inherent torsional resistance due to the tightly stretched bands or springs, was to elevate the center of gravity above the fulcrum by means of a weight, to such a height that the tendency to reach its lowest position (vertically below the center of rotation) almost neutralizes the total resistance. If, therefore, the tendency of the high center of gravity and the resistance of the steel bands or springs are opposed to such an extent as to nearly

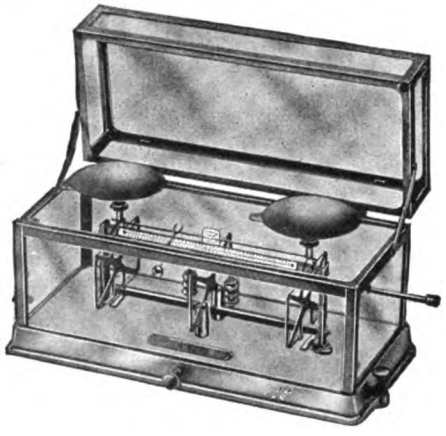


FIG. 10.—Torsion prescription balance.

neutralize each other, the sensitiveness of the balance is established, and the smallest weight placed on the pans will cause the beam to oscillate; on the other hand, the beam will return to its horizontal position by reason of the unneutralized resistance. Recently the weight above the fulcrum has been replaced by two smaller weights, one on each side of the central frame, which serve the same purpose as the single larger weight.

The foregoing principle has been applied to a variety of balances adapted to ordinary commercial weighing, as well as the more delicate adjustment of fine prescription work and chemical analysis; like ordinary balances, they are provided with graduated beams and poise to be used in place of weights. Fig. 10 represents a torsion prescription balance of fine adjustment, with all the parts enclosed in a glass case and fully exposed to view; it is sensitive to 1 milligram or $\frac{1}{64}$ of a grain, and up to 500 milligrams or 8 grains all weights can be adjusted

by means of a rider on the graduated beam. Fig. 12 represents a torsion counter balance sensitive to 2 grains, and having a capacity of 20 pounds; it is also provided with a triple graduated beam for avoirdupois, troy, and metric weights.

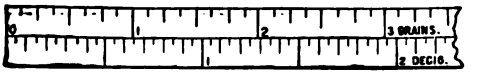


FIG. 11.—Section of rider beam for same.

Every pharmacist who lays claim to doing even a moderate prescription business should have in his possession at least two balances, one of which may be used for weighing quantities ranging from 30 grains to 2 or 3 ounces, and should be sensitive to at least ½ grain;

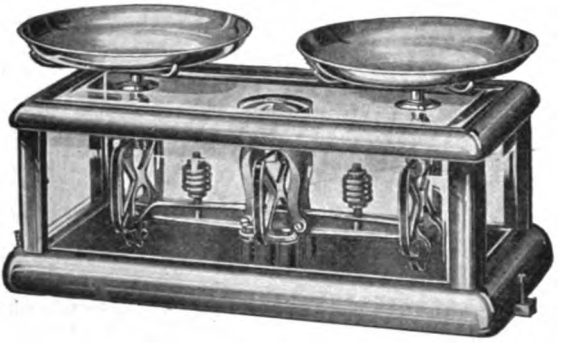


FIG. 12.—Torsion counter scale in glass case.

while the other should be confined to quantities never greater than 2 grams or 30 grains, and should respond readily to a change in weight amounting to 2 or 3 milligrams or $\frac{1}{30}$ to $\frac{1}{20}$ grain; besides these a larger balance (usually termed counter scales is needed for general

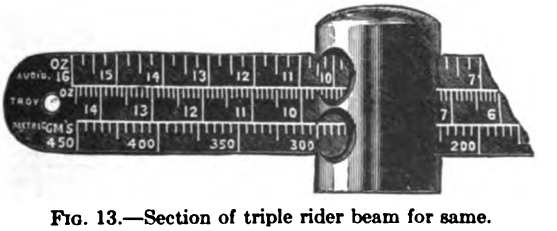


FIG. 13.—Section of triple rider beam for same.

trade; this should be of such adjustment as to allow accurate weighing thereon of quantities ranging from ½ ounce to 5 or 10 pounds, and should be sensitive to 5 or 10 grains with a full charge.

Weights.—Weights are pieces of metal designed to weight aliquot parts of the established units; brass or iron is used for the customary

commercial weights, while brass or aluminum is chosen for weights employed for dispensing purposes; platinum is also occasionally used for small prescription weights on account of its extreme hardness and resistance to atmospheric influences. Accurate weights are as essential as accurate balances, for one is rendered unreliable without the other. The usual form of smaller commercial weights is in sets known as box or block weights, and ranging from ¼ ounce to 5 pounds (Fig. 14). Troy weights, as a mark of distinction from avoirdupois weights, are usually sold in nests of brass cups (see Fig. 15); they run from ⅛ ounce to 8 or 16 ounces, and for use in dispensing prescriptions of lower denominations, from ¼ grain up to 2 ounces, are frequently put up in boxes or blocks as shown in Fig. 16. The smaller dispensing weights are made either of brass or nickel-silver, after the style

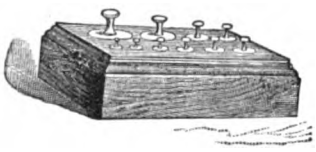


FIG. 14.—Block weights.

FIG. 15.—Set of apothecaries' cup weights.

shown in Fig. 17, or of aluminum if below the denomination of 10 grains (see Figs. 18 and 19); weights less than ¼ grain are often indicated by means of a sliding poise on a graduated beam. The relative lightness of aluminum adapts this metal admirably for use in weights of very low denominations, as they can be made of

FIG. 16.—Apothecaries' weights (¼ gr. to ℥ij) in case.

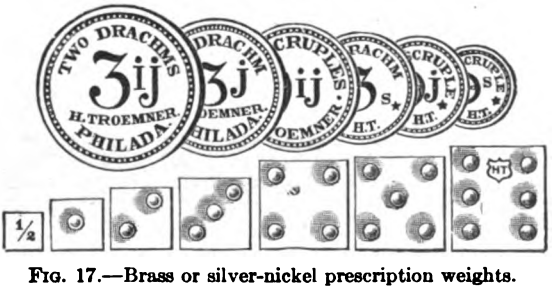


FIG. 17.—Brass or silver-nickel prescription weights.

larger size and consequently be more conveniently handled than heavier brass weights. Metric weights are made of iron, brass, or aluminum, in the same forms as already described for avoirdupois and apothecaries' weight.

In connection with the operation of weighing, the term *tare* is frequently used to indicate the weight of the empty vessel (dish,

box, bottle, or jar) in which the substance (liquid or dry) is to be weighed; *gross weight* is the combined weight of the substance and the container; *net weight* is the weight of the substance alone, obtained by subtracting from the *gross weight* the *tare* of the container. Instead of finding the exact weight of the container, the latter may be simply *counterpoised* or balanced by small shot or dry coarse sand contained in a suitable cup.

FIG. 18.—Aluminum wire weights.

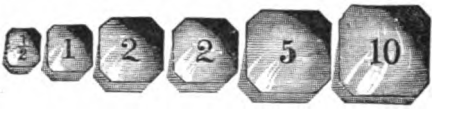


FIG. 19.—Aluminum grain weights.

Everyone who has occasion to use fine balances should early accustom himself to certain habits of care and neatness, which will materially preserve the sensitiveness of the instrument. The following rules are recommended: *Never allow the beam to oscillate when the balance is not in use. Immediately after the operation of weighing is completed replace the weights in their proper receptacle and clean the pans with a soft towel. Never weigh deliquescent salts, or active chemicals, such as iodine, on the metal pans, but always on glass or in*

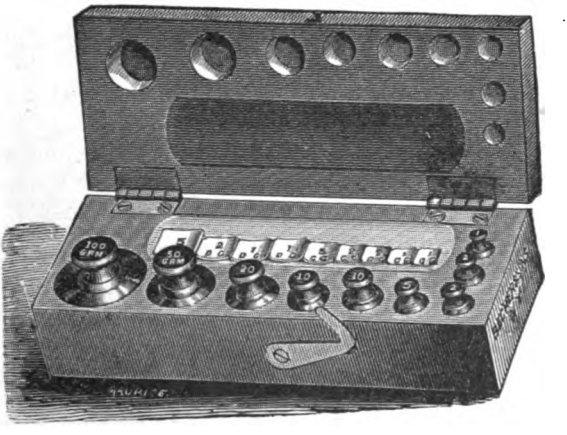


FIG. 20.—Set of metric prescription weights. (100 grams to 1 centigram.)

tared vessels. Always weigh potent or poisonous drugs on stiff glazed paper, using pieces of equal size to counterpoise each other. Never place large weights on the pans, nore remove them, while the beam is in motion as the sudden jar produced by the change causes undesirable friction and destroys the sensitiveness of the balance.

Measures.—Measures are vessels used for determining the volume of liquids, and even dry substances; the latter kind do not concern

the pharmacist, who is compelled, however, to have on hand a variety of vessels provided with appropriate scales of measurement for liquids. Such vessels are made of glass, and are known simply as graduates; they occur of different capacities from 1000 mils. (or Cc.) (1 liter) down to 5 mils. (or Cc.), and from 64 fluidounces down to 60 minims. The *Phœnix graduates*, manufactured in this country by the Whitall Tatum Co., of Philadelphia, are made according to the U. S. standard of apothecaries' fluid measure and bear an inscription guaranteeing accuracy. Since Imperial measure differs materially from U. S. fluid measure, graduates made in England cannot be used in this country unless they have been adjusted according to the American standard. Accurate metric graduates are also now made in this country. *It is as essential to use accurate graduates for measuring fluids, as it is to have accurate balances and weights for weighing dry substances.*

Graduates of different shapes are in use—conical, tumbler-shaped, and cylindrical (see Figs. 21, 22, 23), the last named of which are to to be preferred because more accurate, but are rarely seen in drug stores. Cylindrical graduates have a small diameter, which is uniform throughout the height of the vessel; hence errors in measurement due to capillary attraction are in these reduced to a minimum. They can be had of various volume dimensions, thus for U. S. fluid measure: 60 minims, 2 fluidrachms, 1 fluidounce, and 2, 4, 8, 16, and 32 fluidounces; for metric fluid measure: 5, 10, 25, 50, 100, 250, 500, 1000, and 2000 mils. (or Cc.).

At a Conference on the Weights and Measures of the United States, held at the Bureau of Standards in Washington, D. C. in May, 1916, the conical shape of graduates, as well as the cylindrical, was approved, and the following specifications adopted:

Graduates shall be made to contain or deliver the indicated volume at 20° C. (68° F.) and shall be conspicuously and permanently marked to indicate whether they are graduated to contain or deliver. In the case of cylindrical graduates, the inside diameter of the cylinder shall not exceed one-fifth of the graduated length. The ratio of length of the graduated scale to the internal diameter, in conical graduates, at the highest graduation, shall not be less than 2 to 1, and at one-fourth of the total capacity, this ratio shall not be less than 1 to 1. Graduation marks shall be etched or engraved, but not blown or pressed, and shall not exceed 0.38 mm. (0.016 in.) in width. The clear interval between the graduation marks shall not be less than 1 mm. (0.04 in.).

Tolerances in excess or deficiency on glass graduates were also adopted, based on internal diameter of the graduate, both in metric units and customary U. S. units; they vary from 0.04 mil (or Cc.) for a diameter of 10 mm to 7.1 mils (or Cc.) for a diameter of 100 mm., and from 0.6 minim for a diameter of $\frac{6}{16}$ inch to 2 fluidrachms for a diameter of 4 inches.

The "Acme" graduates, introduced a few years ago, possess the

advantage of being flat on the bottom, without a foot, and hence are less likely to be upset or broken; they are admirably adapted for laboratory work, are cylindrical in form, of about the same diameter

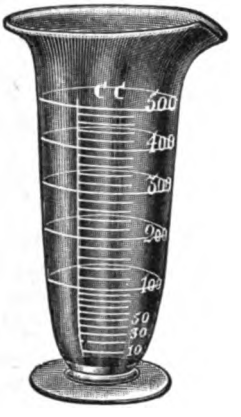


FIG. 21.—Conical graduate.

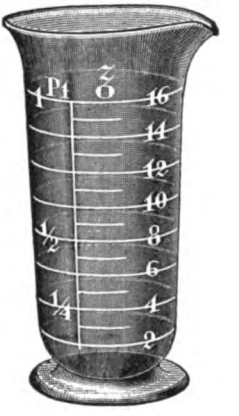


FIG. 22.—Tumbler-shaped graduate.

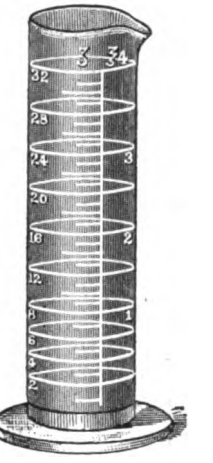


FIG. 23.—Cylindrical graduate.

as tumbler-shaped graduates, and can be had for both metric and apothecaries' fluid measure (see Figs. 24 and 25).

Duplex graduates, arranged for apothecaries' fluid measure on one side and metric fluid measure on the other, are not to be recommended,

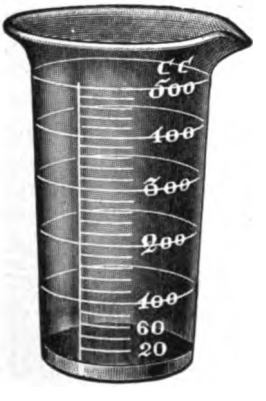


FIG. 24.—Metric fluid measure.

Acme graduates.

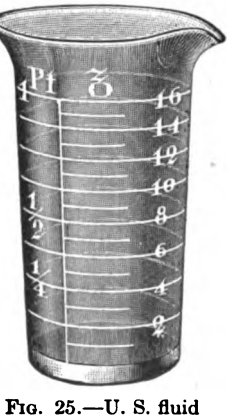


FIG. 25.—U. S. fluid measure.

on account of the danger of confusion and the greater difficulty of accurate measurement.

There is always a slight loss in pouring a liquid from a graduate to another vessel, due to adhesion of the liquid to the glass surface, and

hence pharmacists should use only graduates *calibrated to deliver* given volumes, for it is the fluid measure delivered that is wanted in dispensing work and similar operations. For the preparation of definite volumes of liquids, as in the case of standard volumetric solutions, flasks or cylindrical graduates *calibrated to contain* (*not to deliver*) such volumes should be employed and these should be dry when used.

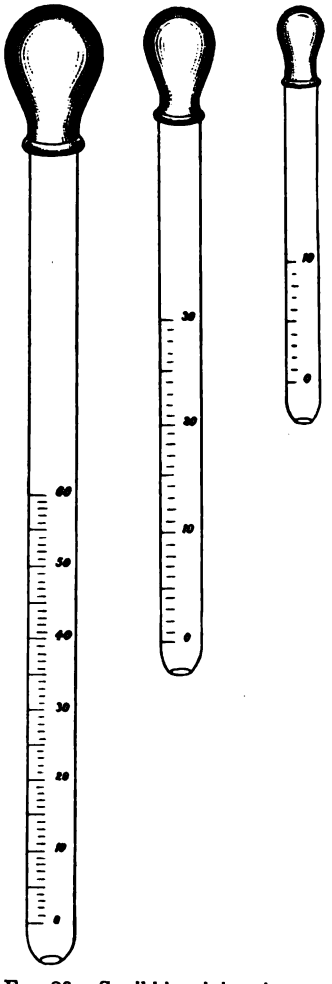


FIG. 26.—Squibb's minim pipettes.

Although minim graduates are extensively employed for measuring volumes of 1 fluidrachm or less, it will be found more desirable and satisfactory to use pipettes graduated to deliver from 5 to 60 minims or from 1 to 10 mils. (or Cc.), the latter being usually graduated into tenths. Such pipettes (see Fig. 26) were first suggested by the late Dr. E. R. Squibb; they are accurately made and can be conveniently kept suspended in a rack made especially for that purpose.

As to the proper manner of holding a graduate while measuring liquids, it may be said that the firmest hold is obtained by grasping the graduate with the left hand in such a manner that the first or index finger encircles the lower part of the vessel, the thumb resting on the base and the second finger forming a support by being placed under the base; this leaves the third and fourth fingers free to remove and hold the stopper of a bottle from which any liquid is to be measured; the mark to which the liquid is to be measured should be on a level with the operator's eye while the graduate is held in an upright position. Owing to capillary attraction, every liquid contained in a graduate will present a concave surface, and the correct reading of a fluid measure is the lower edge of such concave surface, called the meniscus, which should be on a line with the graduation indicating the volume desired.

Graduates which have the same scale marked on both sides, or which are encircled by the markings of the scale, admit of more accurate measurements, and do not require that careful attention to levelling the graduate necessary with the plainer varieties.

Glass graduates are best cleaned by washing with a mop, using soap and water if necessary, rinsing with clear water and allowing the graduate to drain either on a perforated tray or by hanging in a rack; but never should a towel be used to dry the graduate, as it is apt to leave lint adhering to the glass.

Approximate Measurements.—Owing to the varied density of liquids, the number of drops contained in a certain volume must vary greatly with different liquids; moreover, the size of a drop is influenced by the size and shape of the vessel from which the drop is allowed to fall—so that a drop is a very uncertain quantity in the division of doses of medicines. The variability of adhesion to glass exhibited by different liquids, and the rapidity with which liquids flow from the same vessel held at different angles of inclination, are other factors which determine the size of drops, as is shown in the case of chloroform.

Instead of being identical with the minim, drops may vary from one-fifth to one and one-fourth minim.

While our Pharmacopœia does not recognize the drop as an official measure of volume, several foreign pharmacopœias have designated an official dropping tube. In accordance with the International Agreement made at Brussels in 1906, the German, French and Swiss Pharmacopœias recognize a normal dropper having an external diameter of 3 millimeters, which will deliver drops of such size that 20 drops of distilled water shall weigh 1 Gm. at 15° C. (59° F.). The British Pharmacopœia states that the external diameter of the official dropping tube shall be exactly 3 millimeters and that at 15° C. (59° F.) 20 drops of distilled water from this dropping tube are equivalent to 1 milliliter, which is practically identical with the definition of the other pharmacopœias.

For the purpose of better illustration, the following short table has been inserted, showing the great variability in size of drops of different liquids:

TABLE SHOWING THE NUMBER OF DROPS TO A FLUIDRACHM.

Liquid.	120 minims Phœnix Graduate.	1 fluidounce Phœnix Graduate.	W. T. & Co's. exact Medicine Dropper.	Pint or Quart Shelf Bottle.
Distilled Water	48	46	128	
Tincture of Aconite	150	150	190	120
" " Belladonna	144	144	174	108
" " Chloride of Iron	150	150	190	120
" " Opium	130	130	154	
" " " Camphorated	136	136	170	
" " Deodorized Opium	90	110	124	80
Glycerin	90	76	90	
Purified Chloroform	234	240	304	160
" " second trial	274	279	360	180
Dilute Hydrocyanic Acid	60	80	75	60 (℥j bottle)

For the administration of medicines certain familiar domestic measures are employed, which, although subject to considerable variations, are usually estimated as having the following capacity:

A teaspoonful, equal to one fluidrachm;
A dessertspoonful, equal to two fluidrachms;
A tablespoonful, equal to one-half fluidounce;
A wineglassful, equal to two fluidounces;
A teacupful, equal to four fluidounces; and
A tumblerful, equal to eight fluidounces.

Figs. 27, 28, and 29 represent convenient medicine glasses, well adapted to family use.

FIG. 27.

FIG. 28.

FIG. 29.

Graduated medicine glasses.

These vessels are now obtainable accurately graduated and made to correspond to apothecaries' fluid measure; hence they are preferable to the variable tea-, dessert- and tablespoons generally met with, and should be employed altogether in the sick-room.

The U. S. Pharmacopœia states that the following values in metric measure are conventionally attached to the approximate measurements indicated: 4 milliliters = 1 teaspoonful; 8 milliliters = 1 dessertspoonful; 15 milliliters = 1 tablespoonful. These equivalents differ somewhat from those given in the French Pharmacopœia, which are as follows: 1 teaspoonful = 5 Cc.; 1 dessertspoonful = 10 Cc.; 1 tablespoonful = 15 Cc.

CHAPTER III.

SPECIFIC GRAVITY.

A KNOWLEDGE of the subject of specific gravity is of importance to the pharmacist, as it frequently enables him to detect impurities or to determine the identity and quality of the drugs he handles. Specific gravity does not indicate absolute weight, but merely a relative value, or the relation between the volume and weight of bodies as compared with a standard—the standard for liquids and solids being distilled water, while atmospheric air or hydrogen is used for gaseous bodies; in other words, specific gravity expresses the ratio between the weight of any gaseous, liquid, or solid body and that of an equal volume of the respective standard.

The terms specific gravity and density are frequently used synonymously in pharmacy and chemistry. In physics density is defined to be the mass, or quantity by weight, of a substance in a unit volume the latter being either a milliliter (or cubic centimeter), as in the metric system, or a cubic foot, as in the English system. In the metric system, where density expresses the number of grams in a milliliter (or cubic centimeter) of a homogeneous substance, density is identical with specific gravity referred to water at 4° C. (39.2° F.), since the gram is the mass of weight in a milliliter (or cubic centimeter) of water at 4° C. (39.2° F.), and thus comparison with the accepted standard is established. This identity, however, vanishes if the specific gravity has been referred to water at a higher temperature; and although the difference between density and specific gravity at such higher temperatures may not be very great it is sufficient to destroy identity, since 1 milliliter (or cubic centimeter) of water above 4° C. weighs less than 1 gram. In pharmacy and chemistry these slight differences are practically ignored, and hence the terms density and specific gravity are generally used interchangeably, namely, to express the ratio between the mass of a unit volume of water and the mass of a unit volume of the substance being tested. In the English system, where the cubic foot is taken as the unit of volume, density will be expressed by a number 62.4 times as great as the number indicating the specific gravity of a substance at 4° C. (39.2° F.), since a cubic foot of water at 4° C. (39.2° F.) weighs 62.4 pounds, or, in other words, contains 62.4 units of mass. The variations in weight of a cubic foot of water at temperatures above 4° C. (39.2° F.) would have the effect of increasing this ratio (62.4) between density and specific gravity.

As the volume of all bodies varies with temperature, it is essential that the comparison of weights be made at some fixed temperature. On scientific principles and for the sake of uniformity it is desirable that specific gravity always be referred to water at 4° C. (39.2° F.). In some countries this temperature, at which pure water assumes its greatest density is taken for the comparison of weights, while in the United States Pharmacopœia 25° (77° F.) has, with very few exceptions, been fixed as the standard temperature; Great Britain has adopted 15.5° C. (60° F.), and Germany, 15° C. (59° F.). As the comparison of weight of equal volumes of bodies may be made at any temperature desired or convenient, and the specific gravity will vary accordingly, it is necessary to state the temperature in connection with specific gravity; for instance, to say that a liquid has the specific gravity 1.42 would not indicate at what temperature the liquid had been weighed, nor would it indicate comparison with water at any fixed temperature. To say that a liquid has the specific gravity 1.42 at 15° C. would still leave a doubt as to the temperature at which an equal volume of pure water had been weighed for comparison, for it may have been 4° C., 12° C., or even 25° C., and in either case the specific gravity named would not be correctly stated. To say, however, that a liquid has the specific gravity 1.42 at 15° C. *as compared with water at the same temperature,* leaves no room for doubt as to the true ratio existing between the liquid and water—it therefore expresses true specific gravity. The United States Pharmacopœia expressly states that all of its specific gravities are to be considered as taken at 25° C. and *compared with water at the same temperature,* whenever no special temperature is mentioned.

Generally it will be found more convenient to weigh substances at ordinary room temperature, 22° C. (71.6° F.) than to cool them to 4° C. or even to 15° C. and keep them cool while weighing and therefore, assuming that for the majority of pharmacists in the United States a temperature of 25° C. (77° F.) would at all times be more easily attainable and controllable, the Pharmacopœia has adopted this temperature as the official standard for taking specific gravity. This temperature is but very few degrees above the average room temperature, and by using it, the annoying feature of the condensation of atmospheric moisture on the apparatus employed is overcome. The official temperature adopted by the Bureau of Standards at Washington, D. C., for taking specific gravities and similar operations, is, unfortunately, not identical with that of the Pharmacopœia, having been fixed at 20° C. (68° F.).

Whenever a body has been weighed at a temperature different from that at which the standard volume of water has been fixed, it is customary to indicate this difference by writing both temperatures in the form of a fraction, the temperature at which the water was weighed being always written as the denominator and the temperature at which the body being tested is weighed as the numerator; thus,

the expressions 0.927 at $\frac{15°}{4°}$ C., 1.250 at $\frac{15°}{15°}$ C., and 1.340 at $\frac{25°}{25°}$ C., indicate specific gravities found at 15° C. and 25° C., as compared with or referred to water at 4° C., 15° C., and 25° C., respectively.

Barometric pressure is not without effect on the relation between the volume and weight of bodies; hence absolute specific gravity, like absolute weight, is obtainable only *in vacuo;* for pharmaceutical purposes this difference is always ignored and the barometric pressure assumed to be normal, 760 mm. or 30 inches.

The specific gravity of a solid or liquid is always expressed by a number which shows how much heavier or lighter the weight of a certain volume of that solid or liquid is than the weight of the same volume of water; and the specific gravity of a gaseous body is expressed by a number which shows how much heavier or lighter the weight of a certain volume of that gaseous body is than the weight of the same volume of atmospheric air (or hydrogen). The specific gravity of water is therefore stated to be 1, and the specific gravity of air (or hydrogen) is likewise stated to be 1. The following simple rule may be given for finding the specific gravity of any liquid or solid substance by calculation: Divide the weight of a given volume of any liquid or solid by the weight of an equal volume of distilled water, both weighings, if possible, having been made at the same temperature. The quotient expresses the specific gravity.

SPECIFIC GRAVITY OF LIQUIDS.

The determination of the specific gravity of liquids is far more frequently required than is that of solids. The different instruments employed for that purpose are specific gravity flasks or pycnometers, loaded glass cylinders, specific gravity beads, and specific gravity spindles or hydrometers. Any small flask, of 25 or 50 mils. (or Cc.) capacity, with a long, narrow neck and made of thin glass, will answer as a specific gravity bottle. Its weight, or tare, is first carefully ascertained and noted; pure water is then poured into the flask until it reaches a short distance up into the neck, when a mark should be made with a file at the upper and lower edge of the meniscus or concave surface; having noted the temperature of the water, the flask and contents are weighed, and from this weight the tare of the flask is deducted, the remainder being the weight of that particular volume of pure water at the given temperature. The tare, temperature, and weight of water are carefully etched on the side of the flask, which is now ready to be used for taking the specific gravity of any liquid, by filling it to the mark in the neck with the liquid to be tested, then weighing and dividing the net weight of the liquid by the weight of the water, the quotient being the specific gravity of the liquid. Suppose the flask weighs 324 grains and holds, up to the mark, 647 grains of water; filled to the mark with sulphuric acid, it weighs

1511.5 grains, which leaves 1511.5 − 324 = 1187.5 grains as the weight of the acid. Now applying the rule, to divide the weight of a given volume of a liquid by the weight of the same volume of water, the specific gravity is found to be 1187.5 ÷ 647 = 1.835+.

Small glass-stoppered flasks, graduated to hold 100, 250, 500, or 1000 grains of distilled water at 15.6° C. (60° F.), are a more convenient form of pycnometer; they come packed in tin cases, and are accompanied by a metal counterpoise to balance the empty bottle (see Fig. 30). In using these flasks it is necessary to fill them with the liquid to be tested, to a little above the mark in the neck to which the glass stopper reaches when inserted, so that the air and small excess of liquid shall be forced out through the capillary tube drilled through the stopper. The liquid to be tested, having the same temperature as that at which the flask has been adjusted, may be weighed,

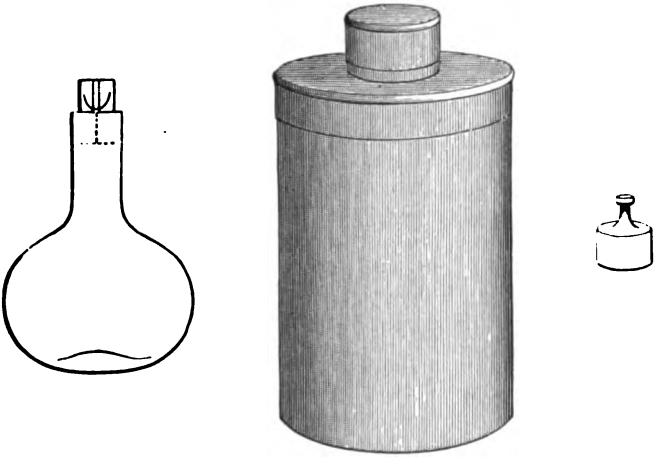


FIG. 30.—Glass-stoppered specific gravity bottle with tin case and counterpoise.

after wiping the flask dry, when, in the case of the 100- or 1000-grain bottle, the weight at once expresses the specific gravity by simply placing the decimal point correctly, without further calculation; for, as the weight of water (100 or 1000 grains) is to the weight of the same volume of any liquid, so is the specific gravity of water (1.000) to the specific gravity of that liquid. Example: If the 100-grain bottle be found to hold 141.5 grains of a certain acid, the specific gravity of that acid will be 1.415; for 100 : 141.5 :: 1.000 : x. x = 1.415.

Some pycnometers are graduated to hold a definite weight of distilled water at 4° C., while others may be graduated at 12° C., 15° C., 15.5° C., 20° C., 25° C., or some other temperature. Hence, if the weighing of other liquids be made in such pycnometers at a higher or lower temperature than the one at which the flask has been graduated, a suitable correction must be made for the expansion or contraction of

water at such temperatures, the change in the glass being usually ignored, since it amounts to but very little. A flask graduated to hold 25 grams of distilled water at 4° C. will hold but 24.979 grams at 15° C., and only 24.9285 grams at 25° C. The cubical expansion of water and other liquids is not uniform for each degree of rise in temperature, and hence a correction by means of an addition or subtraction factor cannot be made. If a pycnometer be graduated at a fixed temperature, and be filled with any other liquid at a higher or lower temperature, the specific gravity of that liquid, as referred to water at such different temperature, can be found only if the weight of a like volume of water at the same temperature as that of the liquid be first ascertained, either by actual experiment or by reference to the subjoined table.

WEIGHT OF 1 MILLILITER OF DISTILLED WATER AT DIFFERENT TEMPERATURES.

At 0° C.	= 0.99988 Grams	At 18° C	= 0.99866 Grams
1°	= 0.99993	19°	= 0.99848
2°	= 0.99997	20°	= 0.99827
3°	= 0.99999	21°	= 0.99806
4°	= 1.00000	22°	= 0.99785
5°	= 0.99999	23°	= 0.99762
6°	= 0.99997	24°	= 0.99738
7°	= 0.99993	25°	= 0.99714
8°	= 0.99989	30°	= 0.99579
9°	= 0.99982	35°	= 0.9944
10°	= 0.99974	37°	= 0.9934
11°	= 0.99965	40°	= 0.9924
12°	= 0.99955	45°	= 0.9904
13°	= 0.99943	50°	= 0.9881
14°	= 0.99930	60°	= 0.9833
15°	= 0.99915	70°	= 0.9778
15.5°	= 0.99908	80°	= 0.9718
16°	= 0.99900	90°	= 0.9656
17°	= 0.99884	100°	= 0.9586

The following examples will serve to illustrate the usefulness of the table:

A flask graduated to hold 25 grams of water at 15° C. (59° F.) is found to hold 22.4 grams of a certain liquid at 25° C. (77° F.); what will be the specific gravity of that liquid at $\frac{25°}{25°}$ C.? A volume of water weighing 25 grams at 15° C. will weigh only $\frac{99714}{99915}$ of 25 grams or 24.949+ grams at 25° C., since 1 mil. (or Cc.) of water at 15° C., weighs 0.99915 grams and 0.99714 grams at 25° C. Then, dividing 22.4 grams, the weight of the liquid at 25° C., by 24.949 grams, the weight of the same volume of water at 25° C., we get 0.89783 as the specific gravity of the liquid at $\frac{25°}{25°}$ C.

A French pycnometer graduated to hold 25 grams of water at 4° C. (39.2° F.) is found to hold 38.75 grams of a certain liquid

at 25° C. (77° F.); what is the specific gravity of the liquid at $\frac{25°}{25°}$ C.? Since 1 mil. (or Cc.) of water at 4° C. weighs 1 gram and but 0.99714 grams at 25° C., the volume weighing 25 grams at 4° C., will weigh only $\frac{99714}{100000}$ of 25 grams or 24.9285 grams at 25° C. Then, dividing 38.75 grams, the weight of the liquid at 25° C., by 24.9285 grams, the weight of a like volume of water at 25° C., the quotient 1.5544+ expresses the specific gravity of the liquid at $\frac{25°}{25°}$ C.

A flask graduated to hold 50 mils. (or Cc.) of water at 15° C., (59° F.) is found to hold 62.5 grams of a certain liquid at 25° C. (77° F.); what is the specific gravity of the liquid at $\frac{25°}{25°}$ C.? Since 1 mil. (or Cc.) of water at 25° C., weighs 0.99714 grams, the flask will hold 50 × 0.99714 or 49.857 grams of water at that temperature; then dividing 62.5 grams, the weight of the liquid at 25° C., by 49.857 grams, the weight of a like volume of water at 25° C., the quoteint 1.253+ expresses the specific gravity of the liquid at $\frac{25°}{25°}$ C.

What will be the specific gravity of a liquid according to the official standard, $\frac{25°}{25°}$ C., if found to be 1.310 at $\frac{25°}{15.5°}$ C.? As the specific gravity 1.310 was found by dividing the weight of the liquid at 25° C. by the weight of a like volume of water at 15.5° C., as indicated by the expression $\frac{25°}{15.5°}$ C., it follows that 1 mil. (or Cc.) of the liquid at 25° C. must have weighed 1.3087948 grams, because it appears 1.310 times as heavy as water, and 1 mil. (or Cc.) of water at 15.5° C., weighs 0.99908 grams (0.99908 × 1.310 = 1.3087948). Now, dividing the weight of 1 mil. (or Cc.) of the liquid at 25° C., 1.3087948 grams by 0.99714 grams, the weight of 1 mil. (or Cc.) of water at 25° C., we have 1.3125+ as the specific gravity of the liquid at $\frac{25°}{25°}$ C.

With the view of overcoming the difficulties usually encountered in regard to temperature, and of insuring more accurate results, the late Dr. E. R. Squibb had constructed a set of specific gravity bottles which are equally well adapted for measuring accurately the standard water volume at any temperature from 0° C. to 25° C., and in which liquids can without loss be brought to room-temperature (or even 25° C., 77° F.) for weighing (see Fig. 31). As seen in the illustration, the bottles may be made of such size as to hold any desired weight of distilled water. They are provided with a long, narrow tube stopper graduated into ½ millimeters from 0 to 50 or 100, to which is attached a safety reservoir fitted with a ground-glass stopper. The capacity

of the bottles is so adjusted that the prescribed weight of recently boiled distilled water will reach to the 0 mark, or a little above it, when the bottle and contents have been kept in a bath of melting ice at 0° C. (32° F.) for fifteen minutes or until the volume ceases to recede. The height to which this same weight of distailled water will rise in the graduated tube at any higher temperature can be readily ascertained by immersing the bottle and contents in a waterbath kept at the desired temperature until the column ceases to rise. By keeping a memorandum of the height of the column in ½-millimeter divisions to

FIG. 31.—Squibb's improved specific gravity bottles.

which the prescribed weight of distilled water will rise at any stated temperature, an equal volume of any other liquid at the same temperature may readily be obtained, accurate adjustment being made by means of very narrow strips of blotting-board passed down the bore of the graduated stem for the purpose of absorbing and removing minute quantities of liquid. Having found the weight of such a volume of any liquid, the specific gravity of that liquid, as compared with water at the same temperature, can be quickly ascertained by dividing the weight found by the prescribed weight of water.

Since glass bottles contract appreciably for two years or more after they have been made, the graduations should be verified every six months or more until contraction has ceased, a memorandum of the changes being kept for reference when the bottle is to be used; thus the point for the volume at 4° C. may have advanced 2 or 3 divisions of the scale, and similarly for any temperature volume. The bottles are always used in a bath of either warmed or cooled water, and when the volume does not change for five minutes, as indicated by the graduated scale, the contents of the bottle may be known to have assumed the temperature of the bath as ascertained by means of a delicate thermometer. A leaden collar is used to keep the bottles steady in the bath.

The cubical expansion differs from different liquids and is not uniform for the same liquid at different temperatures. Tables giving correction factors for ascertaining correct specific gravities at standard temperature are given in the U. S. Pharmacopœia for acetic acid, hydrochloric acid, nitric acid, sulphuric acid, and ammonia water. If the temperature at which the specific gravity has been taken is below the standard, a subtractive correction must be made, and if above the standard, an additive correction. The following examples will serve to show the application of the correction factors:

If a sample of sulphuric acid shows an apparent specific gravity of 1.8145 at 35° C. (95° F.) with a pycnometer standardized at 25° C. (77° F.), an additive correction of 0.0103 must be made, since the Pharmacopœia gives 0.00103 as the correction factor for 1° C. (1.8° F.), for sulphuric acid having the next lower specific gravity at $\frac{25°}{25°}$ C., (77° F.) and the temperature 35° C. is ten degrees above the standard; now $0.00103 \times 10 = 0.0103$, and this, added to 1.8145, gives 1.8248 as the specific gravity at $\frac{25°}{25°}$ C.

If a sample of hydrochloric acid shows a specific gravity of 1.0942 at 20° C. (68° F.) with a pycnometer standardized at 25° C. (77° F.), a subtractive correction of 0.00225 must be made, since the Pharmacopœia gives 0.00045 as the correction factor for one degree C. for hydrochloric acid having the nearest specific gravity to 1.0942 (namely, 1.0960) at 25° C. (77° F.), and the temperature 20° C. is five degrees below the standard; now $0.00045 \times 5 = 0.00225$, and this subtracted from 1.0942 leaves 1.09195 as the specific gravity at $\frac{25°}{25°}$ C.

If a sample of ammonia water shows an apparent specific gravity of 0.9562 at 32° C. (89.6° F.) with a pycnometer standardized at 15° C. (59° F.) an additive correction of 0.00561 must be made, since the Pharmacopœia gives 0.00033 as the correction factor for one degree C., for ammonia water having the nearest specific gravity to 0.9562 (namely, 0.95604) at 15° C. (59° F.), and the temperature 32° C., is 17 degrees above the standard: $0.00033 \times 17 = 0.00561$, which

if added to 0.9562 gives 0.96181 as the actual specific gravity at $\frac{15°}{15°}$ C. This specific gravity is equivalent to about 0.9607 at $\frac{25°}{25°}$ C.

Besides taking the specific gravity of liquids by means of a pycnometer, accurate results may also be obtained with the so-called loaded cylinder. Its use is based on the law formulated by Archimedes, a Greek philosopher, that all bodies immersed in a liquid are buoyed up with a force equal to the weight of the liquid displaced by them, and thus appear to lose weight. For instance, a piece of metal the size of 1 cubic inch, when immersed in water, will exert as much less pressure on the bottom of the container as will equal the weight of 1 cubic inch of water—a fraction over 252 grains—and hence will weigh 252 grains less in water than in air. Floating bodies always displace their own weight of water irrespective of their volume, while immersed bodies always displace their own volume of water irrespective of their weight. All bodies, therefore, which weigh less than an equal volume of water are sure to float in that liquid, only so much of the body being immersed as corresponds in volume to a weight of water equal to the weight of the whole body; on the other hand, all bodies weighing more than an equal volume of water must sink in that liquid and be completely immersed, as the downward pressure of the body exceeds the upward pressure or buoyant force of an equal volume of water.

FIG. 32.—Loaded cylinder.

FIG. 33.—Glass or metal plummet.

The loaded cylinder, as shown in Fig. 32, consists of a glass tube partly filled with mercury, and sealed at the top, to which is affixed a hook for convenient suspension to a scale beam. Having weighed the cylinder in air and then in pure water, at any given temperature, the weight of an equal volume of water is ascertained by subtracting the weight in water from the weight in air; the cylinder is then weighed in any desired liquid at the same temperature as the water, and the loss in weight again noted, which is the weight of an equal volume of that liquid. The volume of the liquid to be tested, being equal to the volume of the cylinder, must be equal to the volume of water also,

for things that are equal to the same thing are equal to each other; by dividing the weight of the given volume of the liquid by the weight of the same volume of water, the specific gravity of the liquid is obtained. Example: A loaded cylinder weighs in air 150 grains, and in water 120 grains, loss of weight in water 30 grains; immersed in sulphuric acid it weighs 96 grains, showing a loss of 54 grains; equal volumes of the acid and water weighing 54 and 30 grains respectively, the specific gravity of the acid must be 1.800, for 54 ÷ 30 = 1.8.

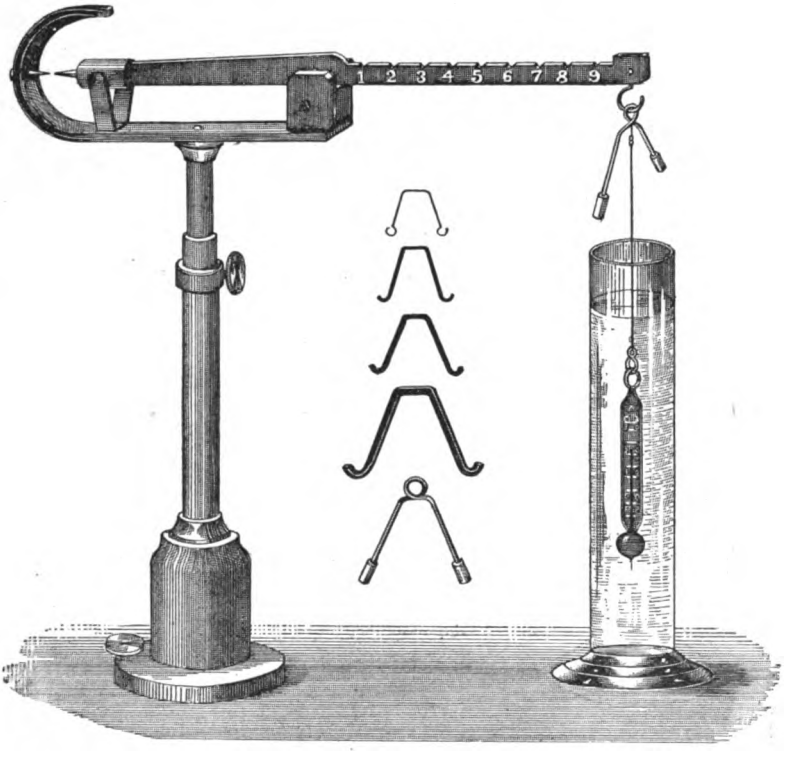


FIG. 34.—The Westphal specific gravity balance.

When only a small quantity of liquid is available for taking the specific gravity the loaded cylinder may be replaced by a small glass or platinum weight of the shape shown in Fig. 33; or Grauer's method may be followed. This consists in using a small pipette having a fine orifice at one end, and at the upper end a short piece of rubber tubing closed by a pinchcock; a mark is made on the glass stem, showing the height to which a convenient quantity of water rises (say 1.0 Gm. or 1.0 mil.), and enough of the liquid to be tested is allowed to rise in the pipette to the mark previously made, the rubber tube is closed, and the whole then weighed; the weight of the liquid in

grams expresses the specific gravity with sufficient accuracy for all practical purposes, as water increases its volume from 4° to 100° C., only to the extent of 0.012, or about $\frac{1}{84}$.

The principle of the loaded cylinder has been utilized in the construction of the Mohr specific gravity balance, of which the Westphal modification is a most desirable improvement (see Fig. 34). The specific gravity of a liquid can be quickly taken at any temperature between 7° and 30° C., since the loaded cylinder has been replaced by a short glass thermometer, which is suspended from the end of the beam by a thin platinum wire; the adjustment having been made at 15° C., a slight variation will be observed for any higher or lower temperature. The small thermometer has a range of twenty-three degrees on the centigrade scale, and, when suspended in air from the longer arm of the beam, establishes perfect equilibrium; when completely immersed in distilled water at 15° C. it displaces its own volume of the water and is buoyed up by a force equal to the weight of the water displaced—equilibrium of the beam being re-established by attaching the necessary counterpoise, which is called 1.000: at 7.5° C. the necessary weight was found to be 1.001, while at 27° C. it was 0.998. As seen in the illustration, the longer arm of the beam is accurately divided into ten even spaces, and the weights, or riders, used to counterbalance the thermometer when immersed in any liquid, are made of brass and aluminum; they are so constructed that each small rider is of exactly $\frac{1}{10}$ the value of the next larger, the largest rider and the counterpoise used to balance the thermometer in water, however, being of the same weight or value. Without the necessity for calculation, if the temperature of the liquid be at 15° C., the specific gravity of the liquid can be at once read off, after the equilibrium of the beam has been established; for instance, in testing alcohol at 15° C., the counterpoise necessary to balance the beam in water will be found too heavy if attached at the same point in alcohol, hence it is removed and the largest rider is placed in the first, or, if necessary, in the second notch on the beam, where it may appear a little too light, and then the smaller riders are added as may be necessary to balance the beam perfectly. The value of each of the two larger riders, when suspended from the end of the beam, is considered as 1.000, while the three smaller riders are valued at 0.100, 0.010, and 0.001 respectively; when removed to the top of the beam the value of each rider is reduced by $\frac{1}{10}$ for every notch. If one of the large riders be placed at the notch marked 8, a second rider at 2, and a smaller rider at 1, the specific gravity of the alcohol must be read as 0.821. In the case of chloroform and all other liquids specifically heavier than water, the large counterpoise is suspended from the end of the beam, and the other riders are placed in the notches as may be necessary; thus chloroform may require all four riders on the beam, the largest at 4, the second at 8, and the smaller two at 9, which would be read as 1.4899 specific gravity.

Whenever two riders of different weight are required in the same notch on the beam, the lighter of the two is suspended from the hook of the heavier, as shown in Fig. 35; thus the specific gravity of liquids can be read with accuracy to four decimal places. The Mohr or Westphal balance cannot be used, however, if only very small quantities of liquid are available, as sufficient liquid is required to immerse the glass thermometer completely.

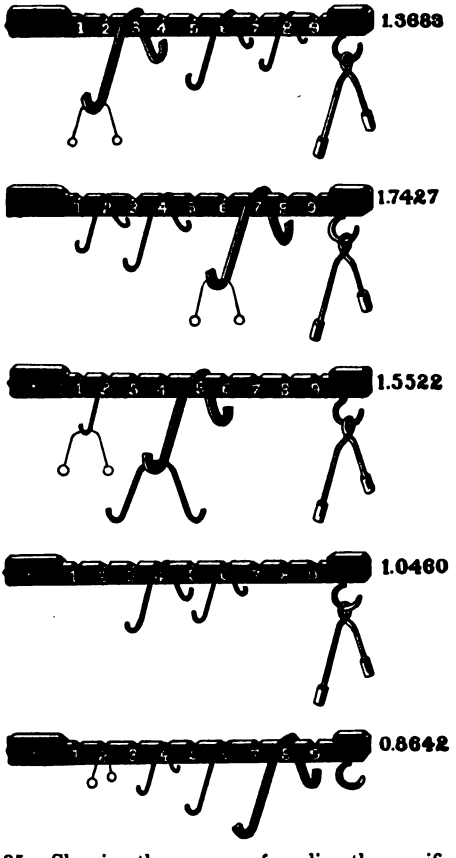


FIG. 35.—Showing the manner of reading the specific gravities.

Specific gravity beads, also known as Lovi's beads, are small, sealed, pear-shaped glass bulbs of various specific weights, which have been carefully ascertained and are marked on them; these beads will float indifferently in any liquid having the same specific gravity, and may be used in adjusting liquids to a fixed specific gravity by dilution or evaporation. If a bead marked 0.93 be placed in a jar of alcohol, it will sink—unless the liquid happens to be official

diluted alcohol—but will slowly rise upon the addition of water, until a sufficient quantity has been added to increase the specific gravity of the mixture to that indicated on the bead, when it will float about midway in the liquid. Results obtained with specific gravity beads are never so accurate as with other methods.

Hydrometers, or areometers, are instruments intended to indicate either the density or the specific gravity of liquids, and in some cases also the percentage by volume or weight of certain liquids. They consist of a glass tube having a bulb blown at one end, a little above which the tube is usually expanded cylindrically for a short distance, and then terminates in a long stem in which is securely fastened a graduated paper scale (see Fig. 36). The bulb is filled with mercury or small shot, so as to enable the instrument to assume a vertical position when floated in any liquid. Hydrometers, like all floating bodies, displace their own weight of a liquid and sink in it to a depth proportional to the volume of liquid displaced, which volume is equal in weight to the weight of the instrument; thus, by comparison of volumes displaced, the densities and specific gravities of various liquids can be ascertained. While the great majority of hydrometers are so constructed that with constant weight they will sink to varying depths in different liquids, some are made to sink to a uniform depth in all liquids by the addition or subtraction of weights, and the density or specific gravity is calculated from such change of weight; this latter class can also be conveniently used for taking the specific gravity of solids.

FIG. 36.—Hydrometer, plain.

Specific gravity hydrometers are made with the unit mark 1.000 at a point to which the instrument sinks in distilled water at *normal temperature* (usually 15.6° C. or 60° F.), and then have the scale carried above and below this point, each mark on the scale indicating either 0.001, or 0.005, or 0.010, according to the intended delicacy of the instrument. As specific gravities of liquids range from 0.700 to above 2.00, the tube of a hydrometer carrying such a scale would have to be inconveniently long to permit a fair reading of it; hence specific gravity hydrometers usually come in sets of four, ranging from 0.600 to 1.000, from 1.000 to 1.400, from 1.400 to 1.800, and from 1.800 to 2.200. When intended for

testing the specific gravity of special liquids the scale is usually much shorter, and thus permits of more accurate graduation.

By far the larger number of hydrometers are intended for determining the density of liquids irrespective of specific gravity; they are extensively employed for technical purposes, and are based on arbitrary scales, no two of which agree, but which can be converted into specific gravity by certain rules. To this class belong Baumé's, Twaddell's, Cartier's, Zanetti's, Sikes', Beck's, Jones', and other hydrometers. Since Baumé's hydrometers are largely used by manufacturing chemists in this country, and the *degrees Baumé* are often stated on labels, the instrument is of special interest to pharmacists.

Baumé devised two hydrometers, one for liquids heavier than water and the other for liquids lighter than water; the former was called *Pèse-Acide*, or *Pèse-Sirop*, and the latter *Pèse-Esprit*. For liquids heavier than water the zero was placed at the point to which the instrument sank in distilled water at 15.6° C., and the point to which it sank in a solution of 15 parts of dry table salt and 85 parts of distilled water, also at 15.6° C., was marked 15; the distance between these two points was then divided into 15 equal parts, called *degrees*, and the scale extended as far as the length of the tube would permit. The zero for liquids lighter than water was found by immersing the instrument in a solution of 10 parts of dry table salt and 90 parts of distilled water at 15.6° C. in such a way that the long stem would be almost entirely out of the liquid; the point to which the instrument sank in distilled water, also at 15.6° C., was marked at 10, the space between the two points being divided into 10 equal parts and the scale extended as in the other case. The slightest error in obtaining the first interval is increased upon extension of the scale; hence it is almost impossible to find two instruments adjusted by the old method to correspond exactly. A more accurate and equally practicable method is to obtain the exact specific gravity of two liquids compared with distilled water at a fixed temperature, place these at the extremes of the scale, and then divide the intervening space into the requisite number of degrees. The liquids chosen in this country, for liquids heavier than water, are concentrated sulphuric acid having the specific gravity 1.8354 at 15.6° C., and distilled water; and for liquids lighter than water, highly rectified ether having the specific gravity 0.725 at 15.6° C., and distilled water; the space between the points to which the hydrometer sinks in the water and the acid is divided into 66 parts or degrees, and the space between the points to which it sinks in the ether and the water into 53 parts. For all liquids heavier than water the scale is read from above downward, while for liquids lighter than water it is read from below upward (see Figs. 37 and 38).

As it is frequently desirable to know the specific gravity for any given degree on the Baumé scale, and *vice versa*, the following rules have been formulated:

For liquids heavier than water: Subtract the degree Baumé from 145 and divide the remainder into 145 to find the specific gravity.

Divide 145 by the specific gravity and subtract the quotient from 145 to find the degree Baumé.

For liquids lighter than water: Add the degree Baumé to 130 and divide the sum into 140 to find the specific gravity.

Divide 140 by the specific gravity and from the quotient subtract 130 to find the degree Baumé.

The moduli or constants employed in these rules which express the proportion borne by the weight of water displaced by the hydrometer when floating in water, to the weight of water equal in volume to one degree, are deduced as follows:

Case I. For Liquids Heavier than Water.—Let a = specific gravity of the lighter liquid, b = specific gravity of the heavier liquid, c = volume of the lighter liquid displaced, and d = volume of the heavier liquid displaced.

The difference between the volumes of the two liquids displaced, as seen in Fig. 39, is $c - d$, indicated by the degrees on the scale to which the hydrometer sinks in the heavier liquid; and hence d, representing the volume of heavier liquid displaced, must be equal to c – the number of degrees.

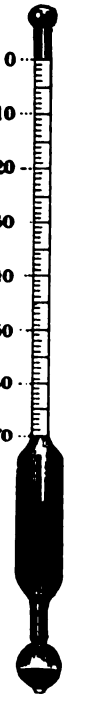


FIG. 37.—For liquids heavier than water.

FIG. 38.—For liquids lighter than water.

The object, first, is to find what relation the volume displaced by the instrument when immersed in water bears to the volume of one degree on the graduated scale, taken as the unit—that is, to find how many degrees on the scale the total volume, c, of lighter liquid displaced, is equal to. The discussion of specific gravity has already shown that the weight of any body is equal to the product of its volume by its specific gravity; hence the weight of water displaced by the hydrometer is equal to the volume displaced multiplied by the specific gravity of water, or equal to $c \times a$; and the weight of heavier liquid displaced is equal to the volume displaced multiplied by its specific gravity, or equal to $d \times b$.

From the law of floating bodies (see p. 59) we know that the weights of the two liquids displaced are the same, being equal to the weight of the hydrometer; and hence it is evident that $c \times a = d \times b$, or $a \times c = b \times d$. Substituting the value of d, as found above, in the equation, we get $a \times c = b \times (c$ — number of degrees), which is equal to $ac = bc - (b \times$ number of degrees). Transposing, we get $-bc + ac = -b \times$ number of degrees, or $bc - ac = b \times$ number of degrees; and factoring, $(b - a)\,c = b \times$ number of degrees, from which it follows that $c = \dfrac{b \times \text{number of degrees}}{b - a}$.

As already stated, distilled water and sulphuric acid of 1.8354 specific gravity are the liquids now used in adjusting hydrometers for liquids heavier than water; and the following numerical values, $a = 1.000$, $b = 1.8354$, number of degrees = 66, can therefore be substituted in the formula just found, when it becomes $c = \dfrac{1.8354 \times 66}{0.8354}$, or $c = 145$, which means that the volume of water displaced by the hydrometer, c, is 145 times as great as the volume corresponding to 1 degree on the graduated scale. The ratio between the two volumes therefore is 145.

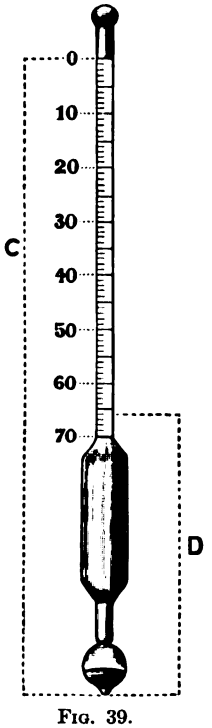


FIG. 39.

The rule for converting the degrees on the hydrometer into specific gravity may be arrived at in the following manner: For equal weights of two substances, the volumes are inversely proportional to the specific gravities. This can be seen from the equation deduced above, viz., $c \times a = b \times d$, which gives the proportion $c : d :: b : a$, since the product of the extremes is equal to the product of the means. From the equation we deduce $b = \dfrac{c \times a}{d}$, or, since $a = 1$, $b = \dfrac{c}{d}$; and since $d = c$ — number of degrees, $b = \dfrac{c}{c - \text{number of degrees}}$. As the value of c has been found to be 145, the specific gravity of the heavier liquid $= \dfrac{145}{145 - \text{number of degrees}}$.

Case II. For Liquids Lighter than Water.—In finding the modulus for hydrometers intended for liquids lighter than water, a slight modification is necessary, as water in this case is the heavier liquid, and consequently a smaller volume of it will be displaced by the instrument. It must also be borne in mind that on the scale for liquids

lighter than water the point to which the hydrometer sinks in water has been fixed at 10 degrees, instead of at 0. As in Case I., let a = specific gravity of the lighter liquid, b = specific gravity of the heavier liquid, c = volume of the lighter liquid displaced, d = volume of the heavier liquid displaced.

By proceeding precisely as in the previous case, we arrive at the same equation, viz., $c \times a = d \times b$ or $a \times c = b \times d$. Hence d, the volume of water displaced, $= \frac{c \times a}{b}$.

As may be seen in Fig. 40, $c - d$, the difference between the volumes of lighter liquid and water displaced, is expressed by the number of degrees difference between the point to which the hydrometer sinks in the lighter liquid and 10, since the water level is at the latter point. The volume of lighter liquid displaced, therefore, is equal to d (the volume of water displaced) plus the difference between c and d—that is, $c = d + (c - d)$.

Replacing the value of c in the equation $d = \frac{c \times a}{b}$, we have $d = \frac{(d + (c - d)) \times a}{b}$, from which we get $bd = ad + (c - d)a$. Transposing we have $bd - ad = (c - d)a$, and by factoring $(b - a)d = (c - d)a$; hence $d = \frac{(c - d)a}{(b - a)}$.

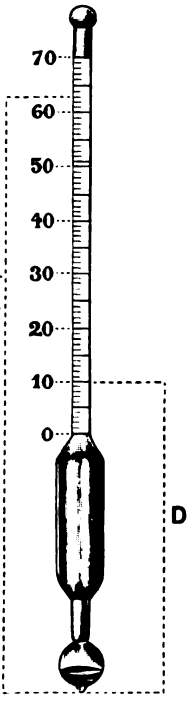


FIG. 40.

As highly rectified ether and distilled water are used in the adjustment of hydrometers, for liquids lighter than water, the following numerical values, $a = 0.725$, $b = 1.000$, $c - d = 53$, can be substituted in the equation, and we obtain $d = \frac{53 \times 0.725}{0.275}$, or $d = 139.7$, which means that the volume of water displaced by the hydrometer bears a ratio of 139.7 to the volume corresponding to 1 degree on the graduated scale; but since the use of 139.7 as the modulus or constant would involve undesirable fractions in applying the rule for conversion into specific gravity, the number 140 has been accepted as the equivalent of d. It is readily seen from the figure that the volume of water displaced by the hydrometer up to the zero mark is $d - 10$ degrees—that is, $140 - 10$, and that c, the volume of lighter liquid displaced, will always be the volume displaced up to the zero mark plus the number of degrees to which the instrument sinks in the lighter liquid—that is, $(140 - 10)$ + the number of degrees, or 130 + the number of degrees.

The rule for converting the degrees on hydrometers for liquids lighter than water into specific gravity, is also deduced from the regular equation $c \times a = d \times b$, or $a = \frac{d \times b}{c}$. Having found numerical expressions for b, c, and d, the formula becomes $a = \frac{140 \times 1.000}{130 + \text{the number of degrees}}$; or the specific gravity of the lighter liquid is obtained by dividing 140 by 130 plus the number of degrees to which the hydrometer sinks.

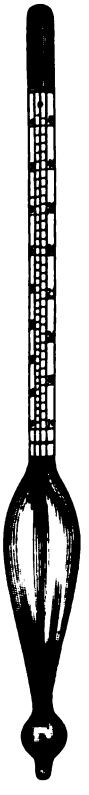


FIG. 41.—Double hydrometer for density and specific gravity determinations.

In order to avoid the use of rules and tables in connection with arbitrary scales, hydrometers have been in use for some years bearing a double scale, for Baumé degrees and the corresponding specific gravity, as shown in Fig. 41: they come in sets, usually five, two of which are intended for liquids lighter than water, and three for liquids heavier than water, the shorter size permitting closer reading within small limits.

The Twaddell hydrometer is only for liquids heavier than water, each degree on the scale being equal to 0.005 specific gravity; hence the requisite number of degrees multiplied by 0.005 and added to 1.000 expresses the specific gravity of any liquid; thus, if a sample of glycerin stands at 50° Twaddell, its specific gravity will be 1.250, for $50 \times 0.005 = 0.25$, and $1.000 + 0.25 = 1.250$.

Nicholson's hydrometer is of the kind intended to sink to a uniform depth (indicated by a mark on the stem) in all liquids by the use of weights, and also possesses the advantage that it can be used for finding the specific gravity of solids as well as liquids. Fig. 42 represents a Nicholson hydrometer floating in a liquid. The construction is readily explained: A is an elongated glass or metal bulb, terminating in a stem surmounted by a metallic disk, B; on the stem is a mark at D, indicating the point to which the instrument must be made to sink; and attached to the bottom of the bulb by means of a small hook, is a loaded cup, C, with finely perforated sides, for carrying solids if so desired. The weight of the instrument complete is marked on the same by the manufacturer, and frequently also the weight which must be placed on the disk B in order to float the hydrometer at D in distilled water. When the latter is omitted, as is sometimes the case, it becomes necessary to ascertain the weight of the volume of water displaced by the hydrometer when immersed to D in distilled water; this is done

by placing sufficient weights on the disk to enable the instrument to float at *D*, and then adding such weights to the known weight of the hydrometer; the sum will represent the weight of water displaced. The weights necessary to sink the instrument to the point *D* in different liquids when added to the weight of the hydrometer therefore represent the weights of equal volumes of such liquids; hence the sum of weights needed for any one liquid divided by the weight of an equal volume of distilled water at the same temperature will express the specific gravity of that liquid. To find the specific gravity of a solid body, first ascertain the weight of the solid body in air by placing it on the pan *B*, and then, having floated the instrument in distilled water, adjusting the weights necessary to sink the hydrometer to *D;* the difference between the weight required to sink the hydrometer to *D* in water, without and with the solid body on the metal disk *B*, indicates the weight of the solid body in air. Now place the solid body in the cup *C* and again adjust the weight; the difference between the present weight and that required when the solid body was on the disk expresses the weight of the water displaced by the solid body; or, in other words, the weight of water equal in volume to the solid body. Finally, divide the weight of the solid body in air by the loss of weight in water, and the quotient will express the specific gravity of the solid body. If the solid body should be lighter in water, and hence float in the same, the cup *C* must be inverted and attached to the elongated bulb by means of the small stirrup under the cup, so that the solid body may be placed underneath of the cup and thus be kept immersed. Solid bodies soluble in water must, of course, be tested in a liquid in which they are wholly insoluble and the specific gravity of which has previously been determined; the calculations for this method are explained on page 74.

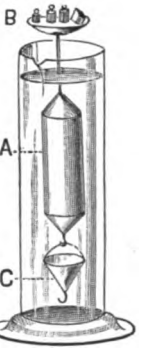


FIG. 42.—Nicholson's hydrometer.

Spirit hydrometers, usually called alcoholometers, are used to ascertain the percentage of absolute alcohol in the commercial article; since the value of alcohol depends entirely upon the amount of absolute alcohol present, this instrument is a most desirable piece of apparatus for pharmacists. Alcoholometers are made of glass, like ordinary hydrometers, but of much longer shape, and are usually provided with two separate scales—Richter's scale, indicating the percentage of alcohol by weight, and Tralles' scale, showing the percentage by volume; since the instrument is adjusted a 60° F. (15.6° C.), it becomes necessary to make proper corrections for any variations in temperature. When immersed in alcohol at normal temperature the figures on the respective scales to which the instrument sinks indicate the number of parts of absolute alcohol contained in 100 parts of the specimen, the

lowest mark on the scale being 0, to which the hydrometer will sink in pure water. Since a cold temperature, by contraction, increases the density of alcohol, the instrument cannot sink as low in the liquid if the temperature be below 60° F. (15.6° C.) as when at 60° F. (15.6° C.); an additive correction in the reading of the scale must therefore be made. On the other hand, if the temperature rise above 60° F. (15.6° C.), the density of the alcohol will decrease and the hydrometer will sink lower, hence a subtractive correction must be made for temperature. The necessary correction has been ascertained to amount to 0.15 for every degree above 60° on the Fahrenheit scale, or 0.27 for every degree above 15.6° on the Centigrade scale. For example, if an alcoholometer sinks in alcohol to 93 on the Tralles' scale at 50° F. (10° C.), the liquid contains really 94.5 per cent. of absolute alcohol by volume, instead of 93 as indicated on the scale, for the temperature is 10 degrees below the normal (60° F.), hence 10×0.15, or 1.5, must be added; but if the temperature had been 70° F. (21.11° C.), the true percentage of alcohol by volume would have been only 91.5; for, the temperature being 10 degrees above the normal, a subtraction of 1.5 from the reading 93 is necessary. Fig. 43 represents a complete alcoholometer carrying a thermometer within the tube for convenience in taking the temperature of the liquid. For testing the specific gravity of urine, a small hydrometer the range of which extends from 1.000 to 1.060 is employed (see Fig. 44); the narrow cylinder in which to float the urinometer was specially designed by Dr. Squibb with the view of preventing the hydrometer from adhering to its sides, by means of the peculiar indentations.

FIG. 43.—Alcoholometer with thermometer enclosed.

Special instruments have been devised for taking the specific gravity of very small quantities of liquids, namely, Eichhorn's areo-pycnometer (Fig. 45) and Rousseau's densimeter (Fig. 46): instead of floating these instruments in the liquid to be tested, the latter is carried in the hydrometer, which is then floated in water. The illustration of the areo-pycnometer shows that it differs in construction from the ordinary hydrometer chiefly in having a glass bulb, *C*, placed between the loaded bulb *F*

and the expanded portion *B* of the stem; the bulb *C* is provided with a stopcock, *D*, and into it is poured the fluid to be tested; the small glass knob *E* serves to balance the instrument when immersed in water, which should be at 17.5° C. (63.5° F.); the specific gravity is shown on the graduated scale on the tube *A*. The densimeter is chiefly intended to be used for oils and similar liquids lighter than water. The upper part of the tube, *A* to *B*, consists of a

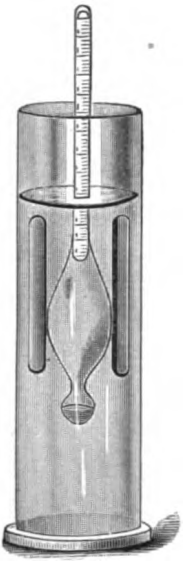


FIG. 44.—Squibb's urinometer and cylinder.

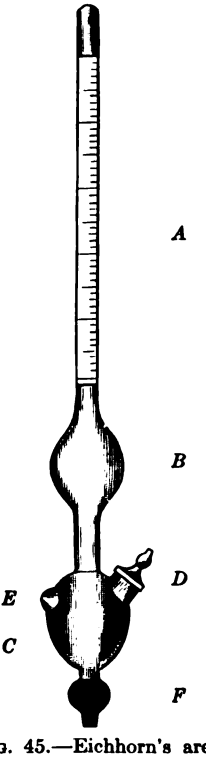


FIG. 45.—Eichhorn's areopycnometer.

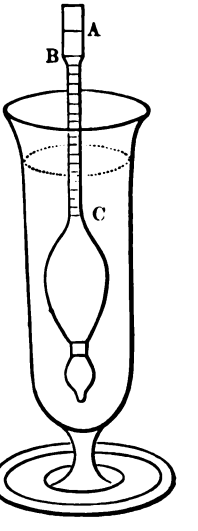


FIG. 46.—Rousseau's densimeter.

little cup of 1 mil. (or Cc.) capacity; when floated in water the instrument sinks to the point *C*, and when carrying 1 mil. (or Cc.) of water in the cup it sinks to *B*. The space on the stem between *B* and *C* is divided into 20 equal parts, each division corresponding to $\frac{1}{20}$ Gm. or 0.050 Gm.; now, if 1 mil. (or Cc.) of oil of peppermint be poured into the cup and the instrument floated in water, it will probably sink to the eighteenth division of the scale; hence $18 \times 0.05 = 0.90$, the specific gravity of the oil.

SPECIFIC GRAVITY OF SOLIDS.

The various methods for finding the specific gravity of solids are based upon the well established principles that all bodies immersed

in a liquid displace a quantity of that liquid equal in volume to the volume of the body immersed, and at the same time are buoyed up with a force equal to the weight of the liquid displaced. The upward pressure exerted by the liquid upon the body immersed causes the latter to appear lighter in weight, and is proportional to the density of the liquid; the loss of weight, then, which a body seems to suffer upon immersion in any liquid represents the weight of a volume of that liquid identical with the volume of the body immersed. As stated on page 51, pure water at 25° C. (77° F.) has been chosen as a standard of comparison for solids, and may be directly employed for the immersion of all bodies upon which no solvent effect is produced; in the contrary case other liquids must be used, as will be shown later on. The specific gravity of any solid can be ascertained by the simple rule of three, provided the first three terms of the proportion are known, namely, first term, the weight of the liquid displaced; second term, the weight of the solid in air; third term, the specific gravity of the liquid used for immersion. Whenever water is used for immersion, the simple division of the weight of the solid in in air by the loss of weight in water (weight of water displaced) expresses the specific gravity of the solid, since the specific gravity of water is 1.000. The methods for finding the specific gravity of solids may be divided as follows:

1. For solids insoluble in, but heavier than water;
2. For solids insoluble in, but lighter than water;
3. For solids soluble in water, whether heavier or lighter than that liquid;
4. For solids in powder form.

For solids insoluble in, but heavier than water, several methods are available; of these, the direct method of weighing is the most accurate and generally employed.

In place of the more expensive hydrostatic balance, any good sensitive prescription balance may be used; the only extra piece necessary being a small wooden or stiff wire bench as a support for the vessel of water as shown in Fig. 47. For instance, a piece of metal is found to weigh 258.75 grains in air; by means of a silken thread, or fine horse-hair, it is completely immersed in pure water and found to weigh 235.75 grains, the difference or loss of weight, 23 grains, representing the weight of a volume of water equal in volume to the 258.75 grains of metal. Dividing 258.75 by 23, the specific gravity of the metal is found to be 11.25.

Another but less accurate method is to weigh the solid by metric weight and then place it in a graduated cylinder containing sufficient water to submerge the solid completely (see Fig. 48); the difference between the first height of the water and that after immersion of the solid indicates the volume of water displaced, and its corresponding weight is readily noted. Suppose a solid body weighing 7.5 Gms., placed into 40 mils. (or Cc.) of water, causes the latter to rise to 41.5

mils. (or Cc.), showing that 1.5 mil. (or Cc.) of water have been displaced, which weighs 1.5 Gms.; then, applying the rule, 7.5 ÷ 1.5 = 5, the specific gravity of the solid.

Since solid bodies will float indifferently in any liquid having the same specific gravity as their own, advantage may be taken of this property to determine the specific gravity of solids. Hager recommends determining the specific gravity of fats by placing them in

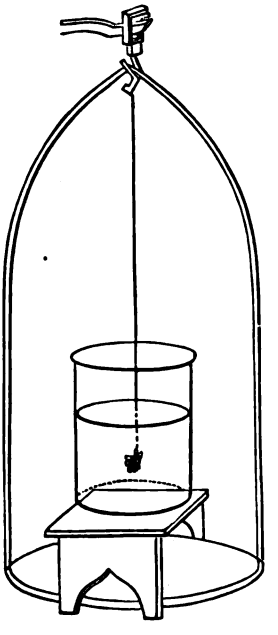


FIG. 47.—Showing the manner of weighing a solid body in a liquid.

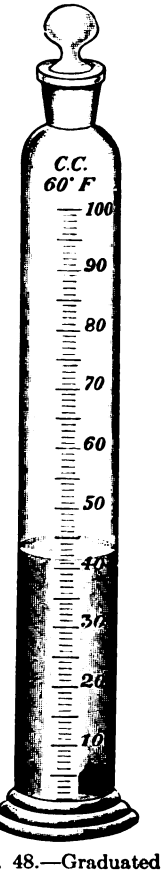


FIG. 48.—Graduated cylinder.

alcohol and then adding water until the fat floats about indifferently beneath the surface of the mixture; the specific gravity of the mixture is then taken in the usual way, preferably by means of a pycnometer, and this at the same time expresses the specific gravity of the solid.

To ascertain the specific gravity of solids insoluble in, but lighter than water, it becomes necessary to insure their immersion in water by attaching to them some heavy substance, the weight of which in water must previously have been ascertained. Upon immersing the

two bodies in water it will be observed that the weight of the two appears less than the weight of the heavy body alone, which is due to the fact that the volume of water equal to the volume of the lighter body is heavier than the latter, and therefore exerts a greater upward pressure on the heavy body, causing it to appear to lose weight. The difference between the weight of the heavy body in water and the united weight of the light and heavy bodies in water expresses the excess of weight of a volume of water over the weight of a like volume of the light body; in other words, it shows how much heavier a volume of water is than the same volume of the light body; to find the exact weight of a volume of water equal to the volume of the light body, this difference, or excess, must be added to the weight of the light body in air. Suppose a piece of cork weighs 62.5 grains in air; attached to a piece of metal which weighs 94 grains in water, the whole is found upon immersion in water to weigh 88 grains, or 6 grains less than the metal alone; adding 6 to 62.5 grains (the weight of the cork) we obtain 68.5 grains, the weight of the water displaced by the cork. The specific gravity of the cork is found by dividing 62.5 by 68.5, according to the general rule on page 53. The answer will be 0.9124+.

For solids soluble in water some other liquid must be selected for immersion, in which the solid body is perfectly insoluble and of which the specific gravity is known; in other respects any of the preceding methods may be followed. In such cases the weight of the liquid displaced, having been ascertained, may be used to find the weight of a corresponding volume of water, and the latter then be divided into the weight of the solid; or the weight of the solid in air may be divided by the weight of the liquid displaced and the quotient then multiplied by the specific gravity of the liquid; by either method the specific gravity of the soluble substance will be obtained. To find the weight of a corresponding volume of water, divide the weight of the liquid displaced by its specific gravity, for the weights of equal volumes of two bodies are to each other directly proportional as their specific gravities. Example: A piece of alum weighs 125 grains in air; immersed in oil of turpentine having the specific gravity 0.860 it weighs 62 grains; 125 divided by 63 (the loss of weight) yields 1.984; oil of turpentine weighing only 0.86 as much as water, 1.984 must be multiplied by 0.860, which gives 1.7062+ as the specific gravity of the alum. Or the weight of a volume of water corresponding to the volume of oil of turpentine displaced may be found by dividing 63 by 0.86, which equals 73.256, and this divided into 125, the weight of the alum in air, also gives 1.7062+ as the specific gravity of the alum.

Sometimes it is desirable to find the specific gravity of solids in powder form, as calomel, reduced iron, lead oxide, and the like; this is best done by using a flask or bottle known to hold a definite quantity of water, introducing a certain weight of the powder, and then filling

with water and weighing the total contents; as two bodies cannot occupy the same space at the same time, it follows that the flask or bottle containing the powder cannot hold the same quantity of water as when empty, and this difference corresponds to the weight of water equal in volume to the powder. Suppose 100 grains of an insoluble powder are placed in a counterpoised bottle capable of holding exactly 1000 grains of water, the latter being then filled with pure water; if the total contents weigh 1088 grains, 12 grains of water have been displaced by the powder, for 1088 — 100 leaves 988, and as the bottle is capable of holding 1000 grains of water, the difference 1000 — 988 = 12 must have been displaced. Then applying the rule, 8.333+ is found to be the specific gravity of the powder, as 100 ÷ 12 = 8.333+.

SPECIFIC VOLUME.

The term specific volume is used to define the ratio existing between the volumes of certain weights of bodies and the volume of the same weight of pure water; it is therefore the opposite of specific gravity. Specific volume is ascertained by dividing the specific gravity of a body into unity, and hence may be called the reciprocal of specific gravity; it may also be found by dividing the weight of a given volume of water by the weight of an equal volume of a liquid. Every pharmacist is aware that it will require vessels of different size to hold one pound of ether, water, glycerin, sulphuric acid, oil of turpentine, or chloroform, and it is often desirable to know in advance the volume of a given weight of a liquid. In the metric system this is a very simple operation, for the weight in grams of any liquid multiplied by the specific volume, or divided by the specific gravity, of that liquid at once expresses the actual volume in milliliters (or cubic centimeters). To find, however, the volume of a given weight, avoirdupois or apothecaries', of a liquid, it becomes necessary first to ascertain the volume of a like weight of water, and then to multiply this by the specific volume, or to divide by the specific gravity of the liquid; or the given weight of a liquid may be divided at once by its specific gravity, which will yield the weight of a volume of water equal to the volume of the liquid, and then by finding the volume of such a weight of water the volume of the liquid is at once known.

Examples: If the volume of 500 Gms. of alcohol U. S. P. is desired, divide 500 by 0.816, the specific gravity of the alcohol, and the quotient 612.74+ will be the answer in milliliters (or Cc.).

To find the volume of 8 ounces of official glycerin (apothecaries' weight) it is necessary to multiply by 480, the number of grains in 1 ounce, and then divide the product by 455.7, the number of grains in one U. S. fluidounce of water, the quotient (480 × 8 = 3840; 3840 ÷ 455.7 = 8.427), 8.427, represents the number of fluidounces contained in the same weight of water; 8.427 then divided by 1.249,

the specific gravity of the glycerin, yields 6.747+ fluidounces as the volume of 8 ounces, apothecaries' weight, of glycerin.

How large a bottle is required to hold 1 pound of chloroform of 1.490 specific gravity? One pound avoirdupois is equal to 7000 grains, and 7000 ÷ 1.490 = 4697.986, the weight in grains of a volume of water equal to the chloroform; then 4697.986 ÷ 455.7 = 10.309, or nearly 10½ fluidounces.

How many fluidounces in 2 pounds of official ether having a specific gravity of 0.715? Two pounds are equal to 14000 grains and in the case of water will measure (14000 ÷ 455.7) 30.72+ fluidounces. The specific volume of ether having a specific gravity of 0.715 is (1.000 ÷ 0.715) 1.3986, and multiplying the volume of 2 pounds of water by the specific volume of the ether, 30.72 × 1.3986, we get 42.965 (practically 43) as the number of fluidounces in the 2 pounds of the ether.

ADJUSTMENT OF SPECIFIC GRAVITY AND PERCENTAGES.

While the adjustment of percentages in liquids as well as solids presents no difficulties, the reduction of liquids from a higher to a lower specific gravity is not quite so easily accomplished, since specific gravity is but the expression of the relation between volume and weight, and condensation of volume generally occurs as the result of a mixture of two liquids. Two very simple rules, or formulas, have been published for the adjustment of specific gravities of liquids, by volume and by weight; but absolutely accurate results are only possible when *no contraction* of volume takes place; in the majority of cases the condensation of volume is but very slight, and for ordinary purposes may be ignored. It is well known that the weights of equal volumes of two liquids are to each other directly proportional as the specific gravities of these liquids; therefore the weight of a liquid divided by its specific gravity represents a weight of water equal in volume to that liquid. It is also well known that the volumes of equal weights of two liquids are to each other inversely proportional as the specific gravities of these liquids; therefore, the volume of a liquid multiplied by its specific gravity represents a volume of water equal in weight to that liquid. The well-known process of *alligation* is admirably adapted to the adjustment of specific gravities of liquids by volume, but is unsuited to adjustment by weight. When two liquids of different specific gravities are mixed, the loss which one suffers will be balanced by the gain of the other; hence the two liquids used must be mixed in inverse proportion to that existing between the gain and loss of specific gravity and the specific gravity of the mixture; the difference between the higher specific gravity and the desired specific gravity of the mixture will therefore indicate the proportion of the liquid having the lower specific gravity; and the difference between the lower specific gravity and the desired specific gravity will indicate the proportion of the

liquid having the higher specific gravity. For example, if solution of ferric chloride, specific gravity 1.520, is to be reduced to 1.387 specific gravity by addition of a weaker solution of 1.280 specific gravity, 107 volumes of the stronger must be mixed with 133 volumes of the weaker solution; or, in other words, 1 volume of the former with 1.243 volumes of the latter. It is customary to set down a problem in alligation in the following manner to facilitate comparison:

$$1.387\begin{cases}1.520 \mid 0.107 = \text{proportion of the stronger liquid.}\\ 1.280 \mid 0.133 = \text{proportion of the weaker liquid.}\end{cases}$$

If a definite volume of the mixture is desired, the requisite volume of the stronger and weaker liquids may be ascertained by dividing the desired volume by the sum of the proportionals, and then multiplying each proportional by the quotient so obtained; thus, if 32 fluidounces are wanted, divide 32 by 0.240 (0.107 + 0.133), which yields 133.3; 0.107 × 133.3 = 14.27 fluidounces, the requisite volume of the stronger solution, and 0.133 × 133.3 = 17.73 fluidounces, the requisite volume of the weaker solution.

That adjustment of specific gravity by weight cannot be made by alligation may be demonstrated by the following example:

Reduce a solution of subsulphate of iron from 1.574 specific gravity to 1.286 specific gravity by addition of water; how much water will be required?

$$1.286\begin{cases}1.574 \mid 0.286 \text{ or } 286 \text{ parts.}\\ 1.000 \mid 0.288 \text{ or } 288 \text{ parts.}\end{cases}$$

Now, if we allow parts to represent grams, we shall have as an answer: Add 288 Gms. of water to 286 Gms. of the iron solution. But this will not make a mixture of 1.286 specific gravity, for 286 Gms. of a liquid of 1.574 specific gravity will measure 181.702 mils. (or Cc.) (286 ÷ 1.574 = 181.702); 288 Gms. of water will measure 288 mils. (or Cc.), making a total volume when mixed of 469.702 mils. (or Cc.), (288 + 181.702), which will weigh 574 Gms. (286 + 288). As the specific gravity of a liquid is determined by dividing the weight of a given volume of that liquid by the weight of a like volume of water, we shall find the specific gravity of the above mixture to be 1.221+ (574 ÷ 469.702 = 1.221+) instead of 1.286, as required.

On the other hand, if we represent parts by milliliters (or cubic centimeters), the resulting mixture of 286 mils. (or Cc.) of iron solution and 288 mils (or Cc.) of water will show a specific gravity of 1.286, as follows: 286 mils. (or Cc.) of the iron solution will weigh 450.164 Gms. (286 × 1.574 = 450.164), and adding to this 288 Gms., the weight of 288 mils. (or Cc.) of water, we have 738.164 Gms. as the weight of the mixture. Then, dividing the weight of the mixture, 738.164 Gm., by the weight of a like volume of water, 574 Gms. (286 mils. (or Cc.) + 288 mils. (or Cc.) = 574 mils. (or Cc.)), we get 1,286 as the specific gravity.

To adjust the specific gravity of a given weight of a liquid to a higher or lower specific gravity, the following formula may be employed:

$$x = \frac{w \times c\,(a - b)}{a\,(b - c)},$$

in which x represents the weight of the diluent, w the weight of the liquid to be diluted, a the specific gravity of the liquid to be diluted, b the desired specific gravity, and c the specific gravity of the diluent. (Whenever water is the diluent, c is made 1.000). As stated before (see above), $\frac{w}{a}$ = weight of water equal in volume to w, $\frac{x}{c}$ = weight of water equal in volume to x, $\frac{w + x}{b}$ = weight of water equal in volume to $w + x$. To find the value of x, the following equation, $\frac{w}{a} + \frac{x}{c} = \frac{w + x}{b}$, must be solved:

$$\begin{aligned} wcb + abx &= wac + acx \\ abx - acx &= wac - wcb \\ x \times a\,(b - c) &= w \times c\,(a - b) \\ x &= \frac{w \times c\,(a - b)}{a\,(b - c)} \end{aligned}$$

Example: How much water must be added to 250 Gms. of solution of potassa of 1.539 specific gravity in order to reduce the specific gravity to 1.036? Substituting numerical values for the letters in the above formula, we have $x = \frac{250 \times 1.000\ (1.539 - 1.036)}{1.539\ (1.036 - 1.000}$; then $\frac{250 \times 0.503}{1.539 \times 0.036} = \frac{125.75}{0.055404} = 2269.6$. Answer: 2269.6 Gms.

To make a definite weight of a liquid of definite specific gravity by mixing two liquids of known specific gravity, both being of the same kind, or one being water:

Let mw represent the desired weight of the mixture, x the weight of the diluent, y the weight of the liquid to be diluted, and a, b, c the specific gravity of the liquid to be diluted, of the mixture desired, and of the diluent, respectively. Since $x + y = mw$, and the value of x has been shown above to be

$$\frac{\text{the weight of the liquid to be diluted} \times c\,(a - b)}{a\,(b - c)},$$

the latter expression may be substituted for x in the equation, $x + y = mw$; thus $\frac{y \times c(a - b)}{a(b - c)} + y = mw$. This simplified is $yca - ycb + yab - yac = mw \times a(b - c)$, and cancelling, $y \times b(a - c) = mw \times a(b - c)$.

$$y = \frac{mw \times a\,(b - c)}{b\,(a - c)}$$

The value of y (weight of stronger liquid) having been ascertained,

it is subtracted from mw, the desired weight of the mixture, to find the value of x, the weight of the diluent.

Example: If it is desired to make 10 pounds of ammonia water of 0.960 specific gravity, from ammonia water of 0.900 specific gravity, mix 3.75 pounds of the latter with 6.25 pounds of water; for, substituting numerical values for the letters in the above formula, the weight of the liquid to be diluted is equal to

$$\frac{10 \times 0.900(0.960 - 1.000)}{0.960(0.900 - 1.000)} = \frac{10 \times -0.036}{-0.096} = \frac{-0.36}{-0.096} = 3.75, \text{ and}$$

$10 - 3.75 = 6.25$.

This example may also be worked out by alligation, which method would give the proportional parts of the volume to be used of each liquid, as follows:

$$0.960 \begin{cases} 1.000 \mid 0.060 \text{ or } 6 \\ 0.900 \mid 0.040 \text{ or } 4 \end{cases}$$

But as weight and not volume is called for, it becomes necessary to find the actual weights of the respective volumes by multiplying the latter by the specific gravities of the liquids; thus,

$$\begin{aligned} 6 \times 1.000 &= 6 \\ 4 \times 0.900 &= \underline{3.6} \\ &\quad 9.6 \end{aligned}$$

The result shows that the mixture would produce only 9.6 parts by weight, and since 10 parts (or pounds) are wanted, the respective necessary quantities may be found by the rule of three; thus,

$$\begin{aligned} 9.6 : 6 &:: 10 : x & x &= 6.25 \\ 9.6 : 3.6 &:: 10 : x & x &= \underline{3.75} \\ & & &\quad 10 \end{aligned}$$

By means of tables published in the U. S. Pharmacopœia the exact percentage strength of certain acids and alkali can be readily determined if the specific gravity of the liquid at standard temperature is known. These tables are arranged in columns, giving the percentage strength, specific gravities at $\frac{25°}{25°}$ C. and $\frac{15°}{15°}$ C., correction of specific gravity for 1° C., fractional percentage strength, etc. The following example will demonstrate the mode of procedure:

What is the percentage strength of a sample of sulphuric acid showing an apparent specific gravity of 1.8230 at 30° C. (86° F.) with a pycnometer standardized at 25° C. (77° F.)?

First find the specific gravity at $\frac{25°}{25°}$ C. by the method already explained on page 58. This will raise the specific gravity from 1.8230 at 30° C. to 1.82816 at $\frac{25°}{25°}$ C., as the additive correction for sulphuric acid of the specific gravity nearest to 1.8230 is 0.001032 for each degree

temperature above standard; 0.001032 × 5 = 0.00516 and 1.8230 + 0.00516 = 1.82816 (rounded off to 1.8282). The nearest lower specific gravity for sulphuric acid in the column for $\frac{25°}{25°}$ C. is 1.8250, showing 92 per cent. of absolute acid in the percentage column. The fifth column of the table gives the fractional per cent. corresponding with a difference in specific gravity of 0.0001; consequently, as the difference between the above specific gravities is 0.0032 (1.8282 — 1.8250 = 0.0032), the fractional per cent. 0.0256, given opposite the specific gravity 1.8250, must be multiplied by 32, and this product 0.8192 (0.0256 × 32 = 0.8192) added to 92, making the percentage of absolute acid 92.8192 in the sample under consideration.

For the adjustment of percentage in alcohol (by weight or volume), in acids (by weight), and in alkali solutions (by weight), the following rules may be applied:

For reducing solutions from a higher to a lower percentage: *Multiply the given quantity by the given percentage and divide by the required percentage; the quotient will be the quantity to which the liquid must be diluted by the addition of water.* Since alcohol is frequently reduced in volume percentage, and contraction of volume invariably follows the admixture of alcohol and water, it becomes necessary, after contraction has ceased, to add sufficient water to restore the original volume of the mixture.

Examples: Reduce 4 pints (64 fluidounces) of 93 per cent. (by volume) alcohol to 65 per cent.: 64 × 93 = 5952, and 5962 ÷ 65 = 91.57. Enough water must be added to the 4 pints of alcohol to yield, after contraction has ceased, 91.57 fluidounces.

Reduce 2 pounds of hydrochloric acid from 31.9 per cent. to 10 per cent.: 2 pounds = 32 avoirdupois ounces; 32 × 31.9 = 1020.8, and 1020.8 ÷ 10 = 102.08. Enough water must be added to the 2 pounds of acid to bring the total weight up to 102.08 avoirdupois ounces.

Reduce 8 troy ounces of stronger ammonia water, 28 per cent., to 10 per cent. strength: 8 × 28 = 224, and 224 ÷ 10 = 22.4. Enough water must be added to the 8 troy ounces of stronger ammonia water to bring the total weight up to 22.4 troy ounces.

For making a definite quantity of a solution of a certain percentage by diluting a stronger solution with water: *Multiply the required quantity by the required percentage, and divide by the higher percentage; the quotient will be the quantity of the stronger liquid necessary, and this, subtracted from the total quantity required, leaves the necessary quantity of water.* When volume adjustment of alcohol is made, the same precautions in regard to contraction of volume must be observed as stated in the preceding rule.

Examples: Make 1 gallon (128 fluidounces) of 60 per cent. (by volume) alcohol from alcohol of 94 per cent. (by volume): 128 × 60 = 7680, and 7680 ÷ 94 = 81.7. Answer: 81.7 fluidounces of the

stronger alcohol must be mixed with sufficient water to yield, after contraction has ceased, 128 fluidounces.

Make 4 pounds of 25 per cent. phosphoric acid from an acid of 85 per cent. strength: 4 pounds = 64 av. ozs.; $64 \times 25 = 1600$, and $1600 \div 85 = 18.823$. Answer: Enough water must be mixed with 18.823 av. ozs. of the strong acid to bring the total weight up to 64 av. ozs.

Make 720 grains of 5 per cent. caustic potash solution from a 12.5 per cent. solution: $720 \times 5 = 3600$, and $3600 \div 12.5 = 228$; $720 - 288 = 432$. Answer: 288 grains of the 12.5 per cent. solution must be mixed with 432 grains of water.

The adjustment of percentage in liquids may also be readily made by the process of alligation, as already explained under adjustment of specific gravities by volume, page 77.

Pharmacists and drug jobbers are sometimes called upon to make mixtures of certain liquids or solids having different percentage strengths in order to produce a desired average strength; this may be done by the general rule for alligation. Write the percentages in a column, and the mean percentage on the left. Connect the simples in pairs, one less than the mean with one greater; take the difference between the mean and the numbers representing the percentage strength of each simple and write it opposite the value with which it is linked. These differences are the relative quantities of the simples taken in the order in which their values stand.

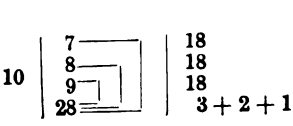
Example: In what proportion may powdered opium of 9, 12.5, 15, and 16 per cent. morphine strength be mixed to produce a mixture of 14 per cent. strength?

		Proof.			Proof.
14	9.0	1.0 1 × 9 = 9	or 14	9.0	2.0 2 × 9 = 18
	12.5	2.0 2 × 12.5 = 25		12.5	1.0 1 × 12.5 = 12.5
	15.0	5.0 5 × 15 = 75		15.0	1.5 1.5 × 15 = 22.5
	16.0	1.5 1.5 × 16 = 24		16.0	5.0 5 × 16 = 80
		9.5) 133			9.5) 133.0
		14			14

Answer: 1 part of 9 per cent., 2 parts of 12.5 per cent., 5 parts of 15 per cent., and 1.5 parts of 16 per cent.; or 2 parts of 9 per cent., 1 part of 12.5 per cent., 1.5 parts of 15 per cent., and 5 parts of 16 per cent.

It matters not how the simples are connected, as long as one less than the mean is compared with one greater, for while the proportional part of each simple may vary, the sum of the proportionals remains the same. If the number of simples is not evenly divided among those less and those greater than the mean, two or more of the former may be linked with one of the latter, and *vice versa;* thus, to mix 7, 8, 9, and 28 per cent. ammonia water so as to produce 10 per

cent. ammonia water, it would be necessary to use 6 parts of the 28 per cent. solution and 18 parts each of the 7, 8, and 9 per cent. solutions.



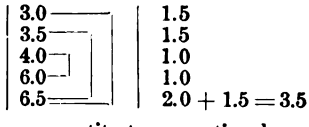
Proof.

18 × 7 = 126
18 × 8 = 144
18 × 9 = 162
6 × 28 = 168
60) 600
10

When the number of simples is uneven, but greater than three, at least two sets of answers are possible as regards the sum of the proportionals.

If a definite quantity of one of the simples be directed to be used in the mixture, the corresponding quantities of the others are readily ascertained by multiplying their proportionals by the ratio which the given quantity bears to the proportional of the simple which it represents.

Example: How much powdered cinchona bark containing 3, 3.5, 6, and 6.5 per cent. total alkaloids may be mixed with 10 pounds of cinchona bark containing 4 per cent. total alkaloids to produce a mixed powder of official strength, 5 per cent. total alkaloids?



10 ÷ 1 = 10, ratio of given quantity to proportional.

Answer.

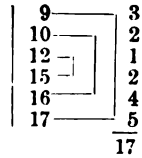
1.5 × 10 = 15 pounds of 3 % bark.
1.5 × 10 = 15 " " 3.5 " "
1.0 × 10 = 10 " " 4 " "
1.0 × 10 = 10 " " 6 " "
3.5 × 10 = 35 " " 6.5 " "

Proof.

15 × 3 = 45
15 × 3.5 = 52.5
10 × 4 = 40
10 × 6 = 60
35 × 6.5 = 227.5
85) 425.0
5

If a definite quantity of a mixture is required, the quantity of each simple may be ascertained by multiplying its proportional by the ratio which the total quantity required bears to the sum of the proportionals of all the simples.

Example: How many grams of powdered opium of 9, 10, 12, 15, 16, and 17 per cent. morphine strength may be taken to produce 520 grams of a mixture containing 14 per cent. of morphine?



17 the sum of the proportionals

3 × 14.706 = 44.118
2 × 14.706 = 29.412
1 × 14.706 = 14.706
2 × 14.706 = 29.412
4 × 14.706 = 58.824
5 × 14.706 = 73.530
250.002

250 ÷ 17 = 14.706, ratio of required quantity to the sum of the proportionals.

Answer: 44.118 Gms. of 9 per cent. opium, 29.412 Gms. each of 10 per cent. and 15 per cent. opium, 14.706 Gms. of 12 per cent. opium, 58.824 Gms. of 16 per cent. opium, and 73,530 Gms. of 17 per cent. opium.

As undesirable fractions are liable to arise in alligation, and integral numbers are always preferable, the adjustment of percentages may be made algebraically, whereby a practically unlimited number of series of correct answers may be obtained and the occurrence of fractions avoided.

Thus in the preceding example, alligation gives a series of fractional quantities which are both impracticable and open to criticism from the standpoint of absolute accuracy. To solve the problem algebraically, we can proceed as follows:

Let a represent the required quantity of opium containing 9 % of morphine.
b " " " " " " " 10 % " "
c " " " " " " " 12 % " "
d " " " " " " " 15 % " "
e " " " " " " " 16 % " "
f " " " " " " " 17 % " "

Then
$$a + b + c + d + e + f = 250; \tag{1}$$
and as the mixture is to be of 14 per cent. morphine strength,
$$\frac{.09a + .10b + .12c + .15d + .16e + .17f}{250} = .14; \tag{2}$$
clearing of fractions, we have
$$.09a + .10b + .12c + .15d + .16e + .17f = .14 \times 250, \tag{3}$$
which is equal to
$$.09a + .10b + .12c + .15d + .16e + .17f = .14(a + b + c + d + e + f); \tag{4}$$
transposing and subtracting, we have
$$-.05a - .04b - .02c + .01d + .02e + .03f = 0. \tag{5}$$
Since multiplying all the terms of an equation by the same number, say 100, does not alter the value of the equation, we may obtain
$$-5a - 4b - 2c + d + 2e + 3f = 0 \tag{6}$$
or
$$5a + 4b + 2c - d - 2e - 3f = 0 \tag{7}$$

In the example given we have six unknown quantities, a, b, c, d, e, and f, and but two conditions, namely, the sum of the quantities must be equal to 250 and the mean of the percentage of morphine in the six different lots is to be 14; hence any four of the unknown quantities may be said to be independent and the remaining two dependent on these four. Now if we assign arbitrary values to four of the unknown quantities, we shall be able by elimination, either by addition or subtraction, to ascertain the corresponding values of the remaining two. As the sum of the six unknown quantities is rather large, 250, it is not wise to assign very low values to any of the four quantities, as this would cause at least one of the remaining values, to be determined, to be undesirably large. If we let $a = 20$,

$b = 25$, $e = 40$, and $f = 60$, and replace these values in equation (1), we have

$$20 + 25 + c + d + 40 + 60 = 250; \quad (8)$$

transposing, we get $c + d = 250 - 20 - 25 - 40 - 60;$

hence $$c + d = 105. \quad (9)$$

Replacing now the same values in equation (7), we have

$$100 + 100 + 2c - d - 80 - 180 = 0;$$

and transposing, $2c - d = 180 + 80 - 100 - 100;$

hence $$2c - d = 60; \quad (10)$$

eliminating d by addition of equations (9) and (10), we have

$$\begin{array}{rl} c + d = & 105 \\ 2c - d = & 60 \\ \hline 3c = & 165 \\ c = & 55 \end{array}$$

If $c = 55$ and $c + d = 105$, then $d = 105 - 55$, which is equal to 50.

The number of grams of opium to be used respectively of the six varieties may therefore be 20 of the 9 per cent., 25 of the 10 per cent., 55 of the 12 per cent., 50 of the 15 per cent., 40 of the 16 per cent., and 60 of the 17 per cent.—total, 250 grams.

Proof:	20 at	9	per cent.	= 1.8
	25 "	10	"	= 2.5
	55 "	12	"	= 6.6
	50 "	15	"	= 7.5
	40 "	16	"	= 6.4
	60 "	17	"	= 10.2
	250 "	14	"	= 35.0

The following table shows a few of the many series possible when different arbitrary values are assigned to four of the six quantities:

9%	10%	12%	15%	16%	17%		14%
4	70	30	17	44	85	=	250
15	10	60	120	20	25	=	250
6	68	32	15	36	93	=	250
6	68	32	12	42	90	=	250
4	72	12	40	74	48	=	250
20	60	40	6	44	80	=	250
24	16	46	92	32	40	=	250
10	20	78	50	40	52	=	250
24	22	40	80	44	40	=	250

CHAPTER IV.

HEAT.

ONE of the most valuable aids to the pharmacist in the numerous manipulations of the store and laboratory is **heat**; hence a knowledge of its varied application and the modes of controlling and directing its influence is necessary.

The undulatory theory regarding heat is now accepted by all scientists; this declares heat to be a force generated by the motion of the molecules of bodies, and that it is the increase or decrease of this molecular energy that give rise to the conditions designated as *hot*, *warm*, and *cold*. No body is entirely without motion of its molecules, hence the terms heat and cold are merely relative; moreover, different bodies have different capacities for heat, as is clearly proved by two persons entering the same apartment, one of whom may complain of uncomfortable warmth, while the other experiences a chilly sensation. The chief effect of heat, or increased molecular motion, is to overcome the force of cohesion and expand the volume of bodies by increasing the intermolecular spaces; the three states of aggregation, known as solid, liquid, and gaseous, being the result of cohesive force, are, therefore, dependent upon the amount of heat generated in or applied to a body.

All solid bodies, when their molecular motion has become sufficiently intensified, will become luminous, as is shown by the spark emitted when steel and flint are struck together, or by the kindling of flame when two pieces of dry wood are rubbed together vigorously for some time.

Oftentimes the luminosity of heated bodies is used to indicate the degree of heat exhibited; hence such terms as dull-red heat, cherry-red heat, and white heat, of which the first named is produced during ordinary combustion of fuel in a stove, without a strong draught of air, while the last named is the result of most intense activity in molecular motion, brought about by the aid of a powerful air-blast in the combustion of fuel or by the use of electric currents.

Heat may be either active or latent; the former increases the temperature of bodies and causes their expansion, while the latter is heat hidden, after the expansion has been effected, for the purpose of keeping up the expansion. Active or sensible heat may be measured by its effect on mercury, upon which latent heat makes no impression; the latter can be converted into the former, however, by pressure and other agencies.

Heat is in almost daily use by the pharmacist in the operations of solution, fusion, evaporation, and decoction, and may be applied either by direct contact with the burning fuel or through the agency of some interposed medium. The use of coal as a fuel for the production of steam is confined to manufacturing establishments, the retail pharmacist finding illuminating gas or some of the various kinds of coal oil better adapted to his wants. Wherever illuminating gas is available it is decidedly the most desirable fuel at the present day, not only because its supply is constant, but also because with modern apparatus and appliances it can be kept completely under control, and thus the greatest amount of heating power be obtained at a minimum of cost. In the course of time electricity will no doubt become an active competitor of gas for heating purposes in pharmaceutical laboratories, as its use in the arts and for domestic purposes has already demonstrated. Fig. 49 illustrates an electric plate-stove, simple in construction and very convenient for boiling and distilling inflammable liquids.

FIG. 49.—Electric plate-stove, showing switch for regulating the current.

Gasoline vapor and kerosene are extensively employed for the generation of heat in localities where illuminating gas cannot be procured; although both are quite cheap in price, a certain element of danger attends the use of the former, while the latter is open to the objections that it cannot be burned without the aid of a wick, that its flame deposits soot unless the wick is carefully watched, and that its conbustion is frequently accompanied by a more or less disagreeable odor. For small operations alcohol offers an excellent fuel of good heating capacity; its high price forbids its more extensive use.

The *amount of heat* produced by the combustion of any particular fuel is constant, no matter how the combustion is effected; but the *intensity of heat* is dependent upon the rapidity of combustion; therefore, the finer the division of the fuel, the more rapidly will it be burned or oxidized, and consequently the greater will be the degree of heat generated.

Various appliances have been designed for the production of heat for pharmaceutical purposes, of which a few are shown herewith, as it is assumed that either gas or coal oil is available everywhere.

When the price of alcohol is not an object, this fuel is preferable to coal oil where illuminating gas is not available. Fig. 50 represents a very convenient form of spirit lamp, nickel-plated and provided with a regulating screw for the wick; it is not easily upset, and answers well for small operations at the dispensing counter.

Barthel's alcohol lamp, Fig. 51, was introduced in Germany in 1891, and is capable of producing an intense heat by the combustion of alcohol vapor. This lamp, which is perfectly safe, is extensively used in Europe; it is made of metal, has a lateral capped orifice for filling, and bears a central tube, closed on top, which carries a solid wick. This is not itself ignited, but only serves to draw up alcohol from the reservoir. To the wick-tube is attached a second tube, the burner-tube proper, which receives the vapors from the wick. The burner-tube contains a wire diaphragm, which can be raised or lowered by means

FIG. 50.—Nickel-plated spirit lamp.

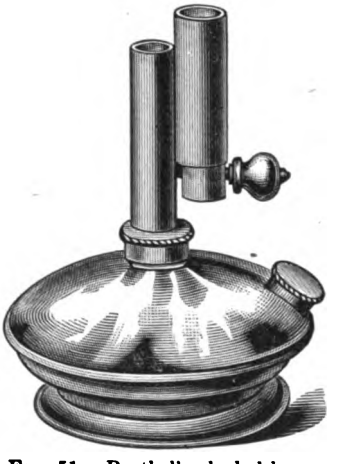


FIG. 51.—Barthel's alcohol lamp.

of the regulating screw, and thus a higher or lower flame obtained as desired. When the lamp is to be used, the wick-tube must be heated slightly by means of a lighted match, so as to drive some alcohol vapor into the burner-tube, where it is then ignited. It will then continue to draw up alcohol vapor of its own accord. The efficiency of the lamp is shown by the fact that a quart of water can be raised from 15° C. (59° F.) to the boiling point in eight and three-quarters minutes, with an expenditure of about 1 ounce of alcohol; low-grade alcohol of 75 or 80 per cent. evaporates less rapidly than stronger alcohol and produces equally good results. Of late years denatured alcohol has been extensively used as a fuel; it serves the purpose well, and, not being subject to Internal Revenue Tax, is of course very much cheaper than ordinary alcohol.

For the combustion of coal oil, stoves are now manufactured which are claimed to produce a smokeless and odorless flame; the heating

capacity of these stoves is quite considerable, and is regulated by means of screws for raising and lowering the wick. Fig. 52 represents the Whitney patent hot-blast stove, in which the wick chamber is separate from the oil reservoir. Coal oil stoves may be had with one, two, or three wicks, and require some attention, so that the wicks shall always be kept well trimmed and free from carbonaceous matter; to avoid a deposit of soot, the wick should never be allowed to touch the vessel to be heated.

FIG. 52.—Whitney's coal oil stove. (Single burner.)

It is well known that the illuminating power of gas depends upon the incandescence of particles of unconsumed carbon, and that if these particles be brought to complete combustion by the appropriate use of air (atmospheric oxygen) the luminosity of the flame will be decreased, but its heating power will be intensified. A yellow carbonized flame, also known as oil flame, because resembling that produced by the combustion of oil, is never well adapted for heating purposes, besides depositing considerable soot or carbon on the bottom of vessels placed over it. In all modern gas heating apparatus proper provision is made for mixing the illuminating gas with such a proportion of air that, when the mixture is ignited, a purely blue flame will result, indicative of complete combustion; the flame of burning alcohol resembles such a flame. A large variety of gas burners and stoves is now offered,

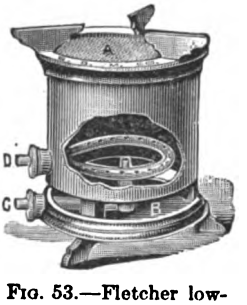


FIG. 53.—Fletcher low-temperature burner.

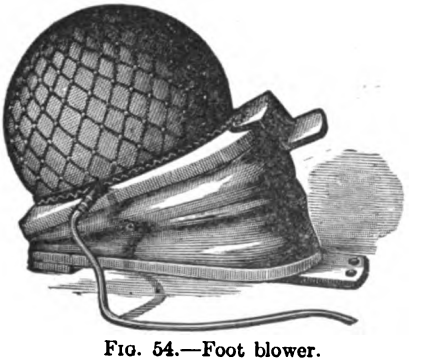


FIG. 54.—Foot blower.

intended to furnish both high and low powers of heat. Of these probably none has a wider range in heating capacity than the Fletcher low-temperature burner (Fig. 53), any degree of heat from a gentle current of warm air to bright red heat being obtainable; it is manufactured by the Buffalo Dental Manufacturing Company, of Buffalo, N. Y. The burner consists of a ring of iron tubing, *D*, perforated on

the upper side, and enclosed in a cylinder of cast iron, over which a diaphragm of wire gauze, *A*, is fastened; there is a space, *B*, between the lower end of the cylinder and the bottom of the apparatus, for the admission of air, and a tube, *C*, for the attachment of a pipe from a bellows when a blast is to be used for producing powerful heat. When a gentle heat is desired, the gas is lighted through the opening *B*, thus heating the air as it flows upward and escapes through the gauze *A*. For a stronger heat the gas and air mixed are lighted above the wire gauze, and a steady, smokeless blue flame is thus obtained. As any rubber tubing attached to *D* is apt to become very hot, it should either be wrapped with a small wet cotton cloth, dipping in water, or, what is still better, about eight inches of gas pipe should be permanently attached to *D*, to which the rubber supply-tube may be secured when wanted. Fig. 54 represents a convenient foot blower for use with any gas furnace requiring a strong supply of air; the rubber disk is well protected by netting.

FIG. 55.—Bunsen burner, low form with crown.

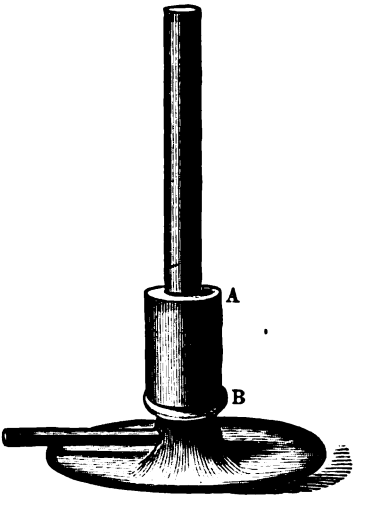


FIG. 56.—The Acme safety burner.

For small operations at the dispensing counter Bunsen burners are usually employed, which are so constructed that a small supply of gas is made to yield a strong heat by admixture with air, whereby perfect combustion is effected. One drawback to some of the Bunsen burners on the market is the tendency to "light back"—that is, when the flame is reduced, it is apt to recede and ignite the gas at the pinhole orifice in the tube; the most effectual method of overcoming this difficulty is to contract the orifice of the tube and introduce a gauze diaphragm into it near the top, which, however, reduces the heating power of the flame. Among the large variety of Bunsen burners sold, a few have been found specially adapted to the needs of the pharmacist, and are here illustrated. Fig. 55 represents a low

form of burner, 3 inches high, made in two sizes, with tubes of $\frac{5}{16}$ and $\frac{5}{8}$ inch diameter, respectively; with the aid of a contracted brass cap the flame can be turned down quite low without receding. When it is desired to distribute the flame the brass crown shown in the cut should be attached, after removal of the brass cap; the crown being provided with three supports, does away with the necessity for a tripod. The burner is made by Bullock & Crenshaw, of Philadelphia, and will be found very serviceable for all smaller operations. In Fig. 53 is shown the Acme burner, patented in 1891 by T. Boyce, of New York; this is probably the most satisfactory burner made for small operations at the dispensing counter, and can be used with coal or gasoline gas. Each burner is provided with two tubes, one of the regular Bunsen pattern, the other with a gauze safety-tip (Fig. 57), permitting the flame to be turned down as low as desired, and out without receding.

FIG. 57.—Gauze tip and tube for the Acme burner.

FIG. 58.—The Finkner burner.

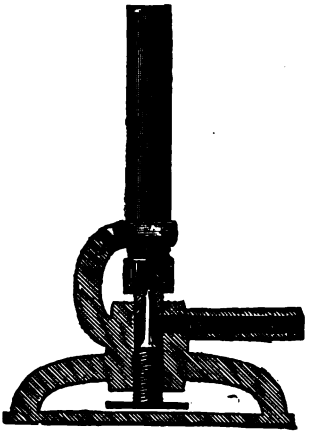


FIG. 59.—Adjustable Bunsen burner.

The supply of gas is regulated by turning the tube at *A* until the desired size of flame is obtained; by turning the milled disk, *B*, up or down, it being threaded and moving upon the nipple, the air-supply is adjusted. The height of the burner is $5\frac{1}{2}$ inches, including the base. The Finkner burner (Fig. 58) yields a very satisfactory flame, but is not adapted for very strong heat; it is so constructed that the supply of gas and admixture of air can be simultaneously regulated by turning the milled head. Fig. 59 represents a convenient adjustable burner; by turning the screw, which is accessible to the fingers while the burner is in use, the gas orifice can be so adjusted that any desired flame may be had. The air supply is adjusted by turning the air-regulator up or down, it being threaded and moving upon the burner tube. The moving of the point up through the gas orifice, while reducing the gas quantity and size of the flame, does not reduce the gas pressure; the gauze safety-tip (Fig. 57) may also be attached to

this burner when a very small flame is desired. For maintaining low temperatures, as in the testing of pepsin and similar operations, the double minim burner (Fig. 60) will be found useful.

For use with inflammable liquids the apparatus illustrated in Fig. 61 will be found serviceable, the burner being surrounded with safety gauze, which prevents the flame from communicating with the vapor on the outside, the principle being the same as in the Davy safety lamps.

Fletcher's radial burner (Fig. 62) possesses some advantages over other heaters in containing no loose parts and in being made entirely of annealed cast-iron; it

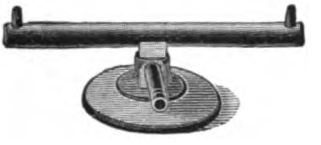


FIG. 60.—Double minim burner.

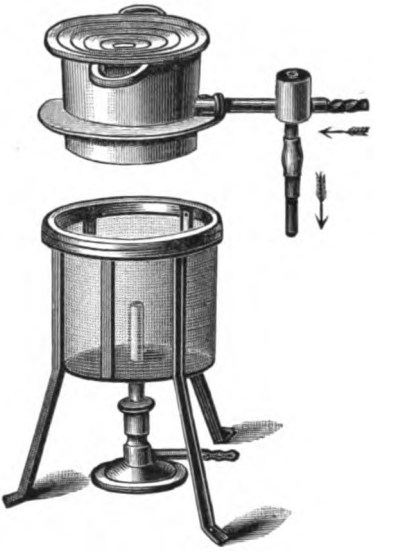


FIG. 61.—Safety burner, to be used for heating inflammable liquids.

is practically indestructible; if choked with dirt, it is readily cleaned with a card or spatula. When in use, the flames are practically *solid* and show no tendency to run to a point in the centre; the consump-

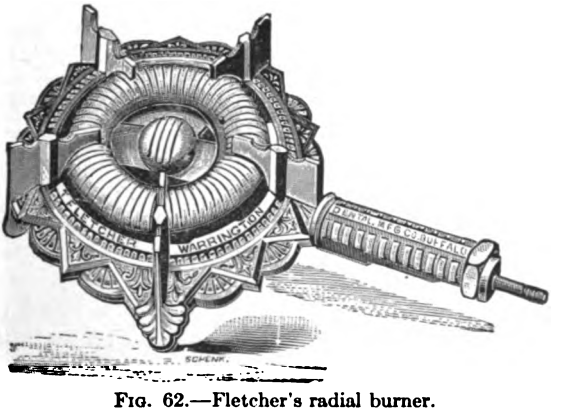


FIG. 62.—Fletcher's radial burner.

tion of gas amounts to from 12 to 18 cubic feet per hour, and the burner will accommodate vessels from 10 to 18 inches in diameter.

For larger operations the "Jewel" gas-stove, Fig. 63, manufactured

by George M. Clark & Co., Chicago, will be found very serviceable. The cast-iron frame is 12 inches square and 5 inches high, thus standing very firm and capable of supporting large vessels. The gas is properly mixed with air before it enters the radial burner, where perfect combustion is effected, as shown by the pale-blue flame, which can be turned down very low without flickering. It consumes about 8 cubic feet of gas per hour, and is a most efficient heater.

For regulating the degree of heat within certain narrow limits, special appliances have been devised, known as thermostats, by means of which the supply of gas admitted to the burner is automatically controlled by expansion and contraction of mercury contained in glass cups or tubes kept in contact with the air or liquid the temperature of which it is desired to maintain at or near certain points. All gas supplied to the burner is made to pass through the thermostat, and the required temperature having been reached, the gauge is set by means of a screw, after which the supply of gas is controlled by the expansion of the mercury caused by an increase of heat. Figs. 64 and 65 show two thermostats frequently employed.

For ordinary operations, quite a fair regulation of

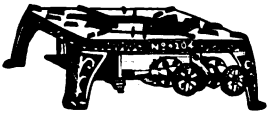


FIG. 63.—"Jewel" gas stove.

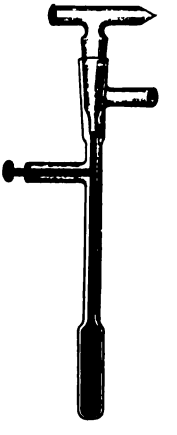


FIG. 64.—Reichert's thermostat.

FIG. 65.—The Bunsen-Kemp gas regulator or thermostat.

temperature can be effected by means of the Hofmann screw compressor (see Fig. 66). The supply of gas being turned on full at the key and the screw having been slipped over the rubber tubing, the latter is compressed until the desired temperature is reached and maintained for some time. This plan is especially effective in connection with an air-bath when a temperature between 110° C. (230° F.) and 115° C. (239° F.) or higher may be desired. For definite lower temperatures between 60° C. (140° F.) and 100° C. (212° F.) the best method for maintaining constancy is by means of the Victor Meyer airbath (see Fig. 67), which is so constructed that liquids of known boiling points, below that of water, are heated in a jacket surrounding an inner compartment. A small quantity of the liquid, 6 or 8 mils. (or Cc.) is put into the outer jacket, and loss by evaporation prevented by means of a long glass tube inserted through the top of the jacket for the purpose of

condensing the vapors and allowing the resulting liquid to flow back. These Meyer airbaths are much used in analytical laboratories, and may be employed for temperatures above 100° C. (212° F.) as well as below.

It is well known that steam, when confined, is capable of absorbing large quantities of heat, and its temperature rises proportionally to the pressure exerted upon it; dense aqueous solutions, therefore, can readily be boiled by means of superheated steam.

For the proper control and distribution of heat, different devices are employed. When direct flame is to be applied to porcelain or glass vessels the interposition of wire gauze or asbestos cloth will be found very desirable; for not only will the heat be supplied to a greater extent of surface by radiation, but at the same time it will be uniformly distributed, and thus insure more regular heating, which of itself is very important, considering the frail character of flasks and dishes. The sandbath is employed for temperatures above that of boiling water, and is chiefly intended to furnish a continuous supply of high heat and to prevent sudden depression of temperature from extraneous causes; it is invaluable in the distillation of certain liquids (acids, etc.) from glass vessels, and may be either of deep or shallow form (see Figs. 68 and 69). The deep sandbath consists of an iron pot or basin containing sufficient dry fine sand so that, if desired, the retort or flask may be entirely surrounded by the same. The best shallow sandbaths are made of Russian sheet-iron, and are well adapted for heating flasks and beakers, which require only sufficient sand to form a good bed of support, since an excessive amount would involve a waste of heat.

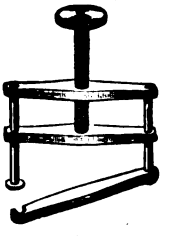


FIG. 66.—Hofmann's screw compressor.

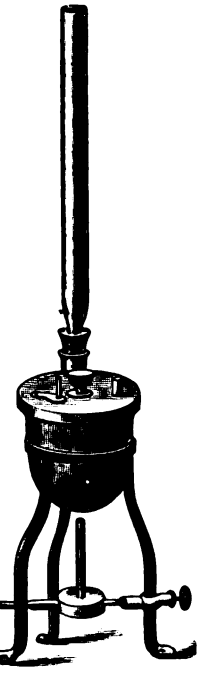


FIG. 67.—Victor Meyer airbath.

For use in a laboratory where steam is available a permanent sandbath may be provided as shown in Fig. 68. It is constructed from an ordinary galvanized iron sink and large gas pipe, about ¾ to 1 inch in diameter, arranged horizontally as shown in the figure. Sand to the depth or 2 or 3 inches may be poured over the pipes, which will form an excellent bed for flasks, dishes, and beakers.

Other apparatus for the use of heat above that of boiling water, yet avoiding contact with flame direct, are oil baths, saline-solution

FIG. 68.—Sandbath, shallow form.

FIG. 69.—Sandbath, deep form.

baths, glycerin baths, or paraffin baths; these are constructed like waterbaths, and readily furnish temperatures ranging from 100° to 300° C. (212° to 572° F.).

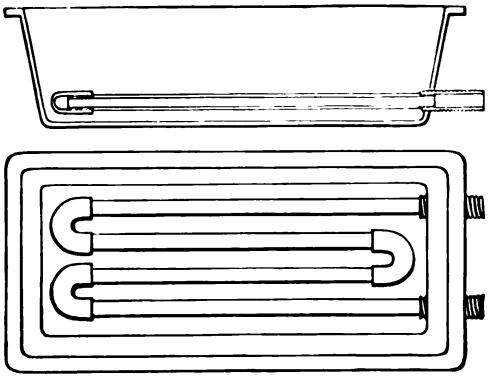


FIG. 70.—Large sandbath, heated by steam.

For all operations requiring a degree of heat below that of boiling water waterbaths will be found indispensable; they may be made

FIG. 71.—Round-bottom waterbath.

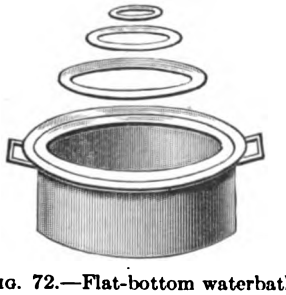


FIG. 72.—Flat-bottom waterbath.

with either a round or a flat bottom, as shown in Figs. 71 and 72, and provided with a set of concentric rings to adapt them for use with dishes or flasks of various sizes. Waterbaths made of extra heavy

tin will last a long time (provided they be dried properly after use), and do not cost much, while copper is far more expensive, but, on the other hand, resists the action of heat and water better than tinned iron. As long as the vapor of boiling water is allowed to escape freely no amount of heat applied to the vessel can possibly increase the temperature of the water above that of boiling, and, as some heat power is lost during transmission from the waterbath to the vessel resting upon it, the liquid contained in such vessel will always be found a few degrees lower in temperature than the water in the bath; under no circumstances can aqueous liquids be made to boil in dishes placed in waterbaths. The name vaporbath is in the majority of cases more appropriate than waterbath, since the vessel heated by it does not, as a rule, come in contact with the water for any length of time, but derives its heat from the vapor or steam rising from the water and not confined by pressure.

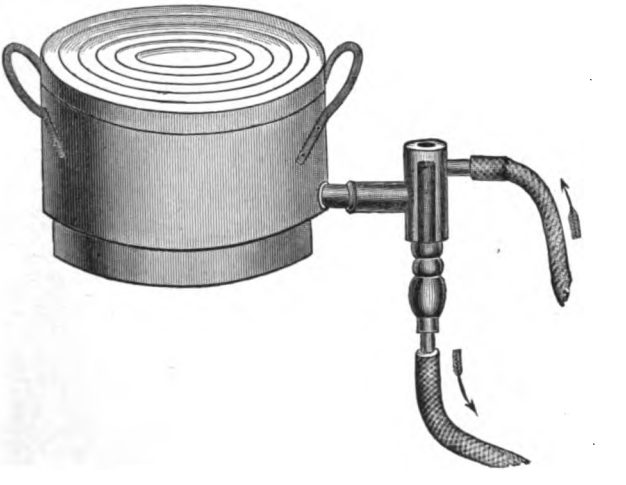


FIG. 73.—Waterbath with constant-level attachment.

The boiling point of a liquid is that temperature at which the elasticity of its vapor overcomes the pressure of the surrounding atmosphere; or, in other words, beyond which it cannot continue as a liquid without increased pressure. Normal atmospheric pressure, 15 pounds to the square inch, which is equal to the pressure of a column of mercury 760 mm. (29.87 + inches) in height, is always assumed when referring to the boiling point of a liquid for any modification of the former will change the latter; thus water, which ordinarily boils at 100° C. (212° F.), has been known to boil at 84° C. (183.2° F.) on Mont Blanc, and even at 35° C. (95° F.) in a vacuum apparatus; while under greatly increased pressure, as in Papin's digester, it has been heated to 160° C. (320° F.) without boiling. There exists also a great variability in the boiling points of different

liquids under normal conditions; for, while official ether boils at about 35.5° C. (96° F.), chloroform requires a temperature of 60.5° C. (140.9° F.), alcohol 78° C. (172.4° F.), glycerin 165° C. (329° F.), mercury about 357° C. (674.6° F.).

The simplest method for determining the boiling point of a liquid is to introduce some of it into a flask provided with a lateral tube in the neck and a thermometer passing through the cork, as shown in Fig. 74, or into an ordinary Florence flask provided with a double perforated cork, through one orifice of which a thermometer is inserted and through the other a bent glass tube, as represented in Fig. 75. If inflammable or noxious vapors are likely to be evolved, the tube

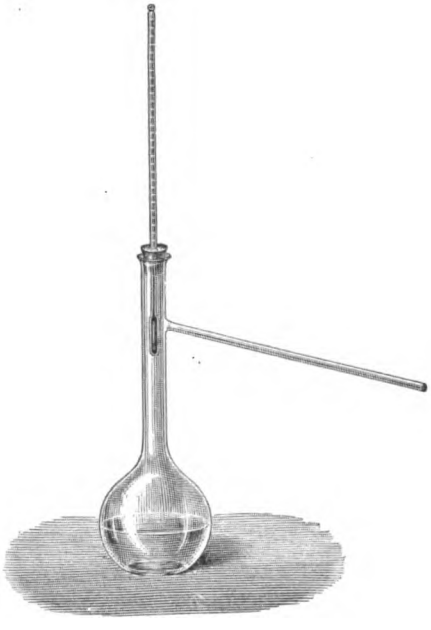


FIG. 74.

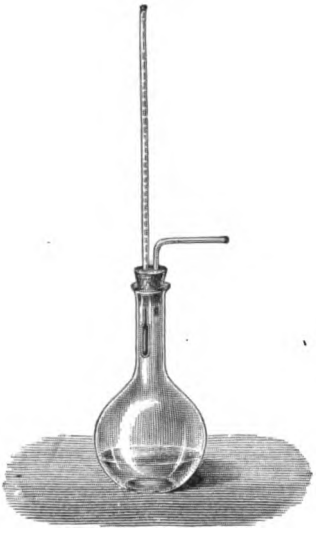


FIG. 75.

Flasks arranged for finding the boiling point of a liquid.

from either flask may be connected with a condenser. It is important that the thermometer should not be immersed in the liquid, but only introduced into the flask so far that the bulb may be enveloped by the vapor of the boiling liquid, as shown in the illustrations. Heat should be carefully applied and gradually increased until the liquid boils actively, at which time the boiling point will be indicated by the height of the mercurial column in the thermometer. In order to avoid errors which might arise from the cooling of the long mercurial column outside of the flask, and the consequent necessity of an emergent stem correction, an accurately standardized thermometer of the Anschütz type (see p. 107) should be used for temperatures above 100° C. (212° F.).

The Pharmacopœia defines the boiling point as that range of temperature within which at least 95 per cent. by volume of a substance distils, when determined by the official method of procedure, as follows: A distilling bulb of from 50 to 60 mils. capacity is recommended, with a neck from 10 to 12 cm. in length and an internal diameter of from 14 to 16 mm.; the lateral outlet tube of from 4 to 5 mm. internal diameter should be attached to the neck at about its midpoint, forming an angle of from 70° to 75° with the lower end of the neck. Twenty-five mils. of the liquid to be tested are introduced into the bulb and after inserting the thermometer (the lower end of which, after having been placed in position, should be 2 to 3.5 cm. below the center of the orifice of the outlet tube), a straight glass condenser from 40 to 60 cm. in length is attached in such a manner that the distance from the upper end of the water jacket to the neck of the bulb shall be from 18 to 25 cm. The bulb is then heated on an asbestos board having a circular perforation located centrally for its reception, and distillation carried on at the rate of 1 mil. every 15 or 20 seconds, noting the temperature as soon as 5 drops of the liquid have distilled into the receiver and again when 95 per cent. of the original volume has distilled. The temperature reading must be corrected for increased or decreased barometric pressure, by subtracting 0.1° C. for every 2.7 mm. increase of pressure, or adding 0.1° C. for every 2.7 mm. decrease of pressure.

Fusible substances when gradually heated to their melting point do not all behave in the same manner; as a general rule, crystallizable bodies become brittle just before melting, while non-crystallizable substances assume a plastic condition. When fusion commences they combine, as it were, with heat in an intimate manner—that is, they occlude heat, so that the further addition of heat does not cause any rise in temperature until all of the substance has become liquefied. The heat thus disappearing is called the latent heat of fluidity, because it is used to change the solid form of a body into the liquid form without any change in the temperature of the body; thus if crushed ice be heated, the temperature will not vary from 0° C. (32° F.) while the ice is melting, and when completely changed to water the temperature of the water will also be 0° C. (32° F.) provided the application of heat be not continued beyond fusion. The amount of heat necessary to produce complete fusion varies with different substances and at different temperatures; thus in the case of ice at 0° C. (32° F.), it has been found equivalent to the amount of heat necessary to raise the temperature of an equal weight of water from 0° C. (32° F.) to 79.25° C. (174.65° F.). This was determined as follows: Two vessels containing respectively equal weights of ice and water at 0° C. (32° F.), and each provided with a thermometer, were heated in a bath of water; at the moment when the ice had completely melted the temperature was indicated as still at 0° C. (32° F.), while the temperature of the water in the other vessel had risen from 0° C. (32° F.) to 79.25° C. (174.65° F.). If 1 pound of ice at 0° C. (32° F.) and 1 pound of water

at 100° C. (212° F.) be mixed so as to avoid loss by evaporation, the result when all the ice has melted will be 2 pounds of water at 10.4° C. (50.7° F.); whereas if 1 pound of water at 0° C. (32° F.) be mixed with 1 pound of water at 100° C. (212° F.), the result will be 2 pounds of water at 50° C. (122° F.). In the first case, 79.25 C. (142.65 F.) degrees of heat were withdrawn from the boiling water to melt the ice at 0° C. (32° F.) into water at 0° C. (32° F.); but in the second case this was not necessary, and the mixture assumed the mean temperature of the two liquids. Physicists express this latent heat of fusion in terms of calories, the word calorie being used to designate the amount of heat necessary to raise the temperature of 1 gram of water from 0° C. (32° F.) to 1° C. (33.8° F.). The latent heat of fluidity of water being known as 79.25° C., a simple rule can be formulated for ascertaining the amount of ice necessary to reduce any given weight of water from a stated temperature to a stated lower temperature, as follows:

Add the desired temperature to 79.25 *degrees centigrade and divide the sum into the difference between the stated temperature of the water and the desired temperature*; the quotient will be the required proportion of ice as compared with the given weight of water.

Example: How much ice is required to cool 1000 Gms. of water from 100° C. to 25° C.?

79.25	100.0	104.25)75.000(0.7194
25.00	25.0	72975
104.25	75.0	20250
		10425
		98250
		93825
		44250
		41700

Answer: 0.7194 of 1000, or 719.4 Gms.

Proof: The ice needs 25° C. in addition to the 79.25° C. required for melting it, and the water loses 75° C. by the reduction of its temperature to 25° C.; as the gain and loss must balance each other, it will require $\frac{75}{104.25}$ of 1000 Gms. of ice, or 791.4 Gms.

The law regarding latent heat of fluidity has a practical bearing upon the fusion of various substances liable to be injured by exposure to a temperature a little above their melting points; thus, a pan of ointment or plaster may be kept over a direct fire without danger of injury *as long as a portion of the contents remains unmelted*, as the increased amount of heat is utilized in the change of the state of aggregation.

The melting points of solids are as variable as are the boiling points of liquids; thus, while ice melts at 0° C. (32° F.) and lard at 39° C. (102.2° F.), sulphur requires a temperature of 115° C. (239° F.) and pure morphine a temperature of 255° C. (491° F.).

The Pharmacopœia defines the melting point as that interval of temperature within which substances are observed to be melting when determined by the official methods, substances to be tested being divided into two classes: Class *A*, substances readily reduced to powder; Class *B*, substances not readily reduced to powder, such as fats, paraffin, wax, etc. The official directions and the apparatus recommended are practically identical with those suggested by G. A. Menge of the U. S. Hygienic Laboratory at Washington, D. C.

Fig. 76 represents the apparatus officially recommended. The container for the bath (*a*) consists of a simple round-bottom straight glass tube of 30 mm. internal diameter, about 100 mm. long and flaring at the top like an ordinary test-tube. Its walls should be not more than 1.5 mm. thick at any point and the tube must be made of glass which will stand heating over a naked flame. The tube is fitted with a stirring device (*b*), which can be made from a piece of small-sized, thick-walled capillary glass tubing about 2 mm. internal diameter. When in use the container is filled with the liquid selected for the bath (for temperatures up to 200° C. pure concentrated sulphuric acid, and for higher temperatures very pure cottonseed oil, or pure recently distilled paraffin, or a mixture obtained by boiling together under a hood for 5 or 10 minutes 70 parts of pure concentrated sulphuric acid and 30 parts of potassium sulphate until perfect solution is effected) to a depth which will permit of such immersion of the bulb of the thermometer that the upper end of the bulb will be 2 to 3 cm. below the surface of the bath and the lower end of the bulb about equally distant from the bottom of the container. As shown in the illustration, the container and thermometer may be conveniently clamped to an ordinary iron stand. The glass tube (*c*) held by the clamped cork (as shown at the top of the figure) and through which the thermometer passes, simply serves to prevent swinging of the thermometer that might be caused by stirring.

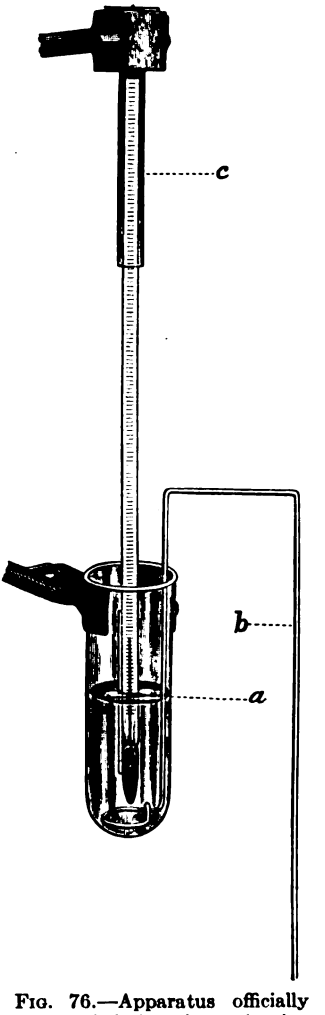


FIG. 76.—Apparatus officially recommended for determination of melting points.

Substances belonging to Class *A* must be reduced to a very fine powder (No. 100) and rendered anhydrous, either by drying at a given temperature if they contain water of crystallization, or by drying for twenty-four hours, over sulphuric acid in a desiccator. A capillary glass tube 6 cm. long and from 0.8 to 1.2 mm. internal diameter, the walls from 0.2 to 0.3 mm. thick, and closed at one end, is charged with sufficient of the dry powder to form a column from 2.5 to 3.5 mm. high when closely packed by moderate tapping of the tube. This is then attached to a standard thermometer by wetting both with the liquid of the bath, or by means of a piece of platinum wire, in such a way that the substance is centrally located by the side of the bulb. Having immersed the thermometer and tube in the liquid selected for the bath heat the latter by means of a free Bunsen flame until a temperature 25° C. below the supposed melting point is reached, then carefully regulate the rate of rise in temperature to about 3 degrees per minute until the substance begins to melt. The temperature at which the column of the substance definitely collapses against the sides of the capillary tube at any point is defined as the beginning of melting and the temperature at which the substance becomes liquid throughout is defined as the end of melting. The bath must be stirred constantly during the time of heating in all cases.

For substances belonging to Class *B*, not readily reduced to powder, a capillary tube open at both ends must be used. The substance to be tested is carefully melted at as low a temperature as possible and drawn into the tube to a depth of about 10 mm. The charged tube is then cooled at 10° C. or lower for twenty-four hours, or in contact with ice for two hours, and attached to the main thermometer by means of a rubber band, adjusted and heated in a waterbath in the manner directed above for substances of Class *A*, except that within 5 degrees of the assumed melting temperature, the rate of rise of temperature is carefully regulated to about 0.5° per minute. The temperature at which the substance rises in the capillary tube is taken as the melting point.

Standardized thermometers only should be used in order that calibration corrections may be applied to the observed readings. Correction must also be made for the emergent stem of the thermometer if strictly accurate results are desired. For this latter purpose an accurate auxiliary thermometer is attached to the main thermometer at a point midway between the surface of the bath and the supposed melting point, in such a manner that the center of its bulb is as close as possible to the stem of the main thermometer. The correction for emergent stem is made by application of the following formula (known as the Kopp formula): Correction = 0.000154 (0.00015 U. S. P.) × N (T–t) in which T represents the temperature registered by the main thermometer; t, the mean temperature of the emergent stem as measured by the auxiliary thermometer (*i. e.*, the temperature at a point midway between the surface of the bath and the top of

the mercury thread of the main thermometer; N, the length of emergent stem measured in degrees (*i. e.*, if the main thermometer is immersed in the bath to the 10 mark and the temperature is 200° C., then N = 200 — 10 or 190).

The simple apparatus shown in Fig. 77 is intended to insure uniformity in heating the mercurial column of the thermometer by suspending the latter in a tube enclosed within another filled about ¾ with sulphuric acid. The temperature of the air surrounding the thermometer in the inner tube is kept fairly uniform by circulation of the acid fluid

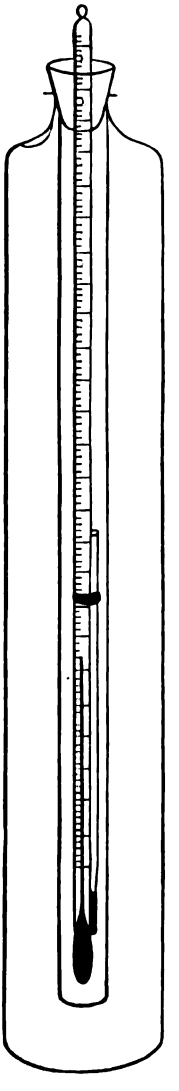


FIG. 77.—Simple apparatus for the determination of melting points.

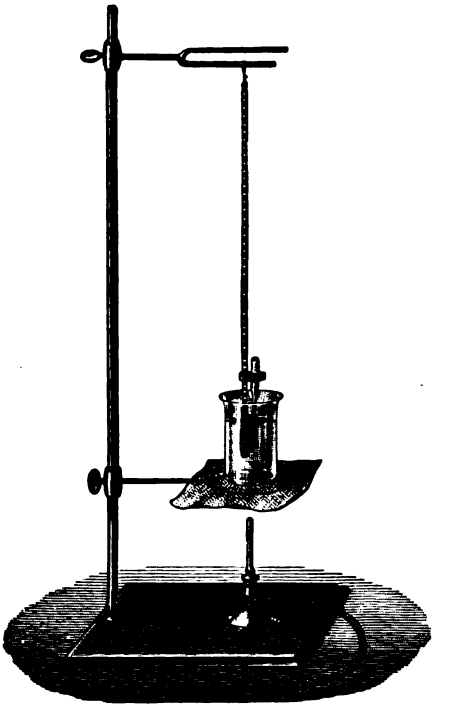


FIG. 78.—Old method of finding the melting point of substances.

in the outer tube when heat is applied, and the results are more accurate than those obtained by the old method shown in Fig. 78, now rarely used.

The term *temperature* is used to designate *intensity* but not *quantity* of heat, which is measured by a thermometer, an instrument consisting of a narrow capillary tube of uniform bore, hermetically sealed at the upper end and terminating below in a bulb of glass. The bulb and a portion of the tube are filled with mercury (in some cases with colored alcohol or toluene), and the whole is provided with a graduated scale for measuring the rise and fall of the liquid within the tube; mercury is preferred for all temperatures not below —40° C. (at which point it freezes), on account of its non-adhesion to the sides of the glass tube and consequent convex surface, and its great sensitiveness to even the slightest change in temperature. Absolute alcohol, although admirably adapted for very low temperatures, cannot be used for measuring heat intensity above 78.3° C. (172.9° F.), its boiling-point. The space above the liquid in the tube is deprived of air, so as to insure the ready and uniform rise of the liquid when expanded by heat.

As all glass vessels continue to contract for some time after they have been made, absolutely correct measurement of temperature can only be obtained if the error of the thermometer is known and then applied for correction of the reading. Clinical thermometers, used by physicians for taking the temperature of fever patients, should invariably be supplied with a certificate showing their error, as this may in some cases amount to nearly ½ degree. Since 1901 the U. S. Government has had in operation a Bureau of Standards in the Department of Commerce at Washington, D. C., where clinical thermometers may be examined and certificated. The following is the method pursued: After careful examination for defects of construction, the thermometer is compared with the standard thermometers of the bureau at the four test-points 96°, 100°, 104°, and 108°, two independent comparisons being made at each point. If the two tests at any point differ by more than 0.15° F., or if the mean of the two tests gives a correction in excess of 0.3°, the thermometer is rejected. Moreover, errors in the intervals between test-points must not exceed 0.3° F.; for example, if the correction at 96° is 0.3°, and at 100°, 0.1°, the error in the interval would be 0.4°, and the thermometer would be rejected. Careful examination of the index is also made, and if upon trial, by means of a special whirling device, the index fails to return to its original position, showing that it is too difficult to shake down, the thermometer is rejected. The results of these examinations, in tabulated form, are furnished the applicant who submits the thermometers, and thus the exact error of each theromometer becomes known. Pharmacists who supply physicians with clinical thermometers should demand that each instrument be supplied with a government certificate. All clinical thermometers should be "seasoned" or "aged" for a year or two before they are examined, so that any error found may remain constant.

Experiments made by the Bureau of Standards have shown that where ordinary domestic glass is used in making all parts of the

thermometer, the average increase in the reading at the end of two months is 0.3 of a degree, and at the end of fourteen months 0.68 of a degree. If French hard glass or Jena normal glass is used, the average change in the reading at the end of two months has been found to be only 0.06 of a degree, and at the end of fourteen months 0.11 of a degree. Some manufacturers of thermometers now make the bulb of hard glass (because the contraction of this part of the instrument causes the greatest error) and the stem of softer glass.

Since 1893 thermometers of great accuracy, intended for very high temperatures, up to 550° C. (1022° F.), have been made in Germany, of special glass, known as "Jena resistance glass", which is very hard and non-contractile. In order to prevent boiling of the mercury, which ordinarily occurs at about 357° C. (674.6° F.), the capillary tube is expanded at the upper end and filled above the mercurial column with compressed dry carbon dioxide. Thermometers of still higher range have been manufactured in which the indicator consists of an alloy of sodium and potassium, instead of mercury, and which may be used for temperatures as high as 650° C. (1202° F.). The alloy is also enclosed in "resistance glass," and the space above the alloy is filled with nitrogen at such pressure that when the bulb becomes red-hot the pressure inside is equal to that of the atmosphere. The glass of the bulb is attacked by the alloy and stained brown; but this occurs at the time of filling, and the coating then formed upon the surface of the glass protects it from further action.

For registering still higher temperatures, instruments known as pyrometers are employed, which are, however, not very trustworthy; they are of two kinds: Wedgwood's pyrometer, based on the contraction of clay, and Brogniart's pyrometer, based on the expansion of metals. When it is desired to note the highest or lowest temperature reached during any fixed time, maximum and minimum thermometers, so constructed that a small metallic or glass indicator is carried to the highest point when the volume again changes, are used.

Three different thermometric registers, known as the Fahrenheit, Réaumur, and centigrade scales, are in use. The centigrade scale is used in France, and is now universlly employed for scientific purposes, while the Fahrenheit scale is in common use in this country and Great Britain, and the Réaumur scale is ordinarily used in Germany. The graduations of all three scales are arbitrary, yet based upon careful observations of their respective authors. Fahrenheit, a German, who, while living in Holland, invented the mercurial thermometer in 1714, divided his scale ranging from 0° to 96°, according to three fixed points. The first point, marked zero, was found by noting the level to which the mercury fell in the thermometer when the instrument was immersed in a mixture of water, ice, and ammonium chloride (or sea salt), supposed at that time to produce the greatest cold attainable. The proportions used by Fahrenheit for this experiment are unknown, and have not been duplicated since. The second

point was obtained by placing the thermometer in a mixture of ice and water or in melting ice, and indicated the level to which the mercury fell when thus immersed. This point was called the beginning of freezing, and corresponded with the 32d division of Fahrenheit's scale. The third point was that reached by the mercury upon introducing the thermometer into the mouth of a healthy man, and holding it there for a few minutes. The scale was afterward extended to 600°. The origin of the degree 212 for boiling water was probably accidental, since Fahrenheit does not appear to have used the boiling point of water as a fixed point, and had no intention of dividing the interval between his zero and the boiling-point of water into 212 parts. It is probable that the 212th division on Fahrenheit's scale, after extension, happened to coincide with the level of the mercury in the thermometer at the boiling-point of water. The present Fahrenheit scale is evidently not identical with the original, but the result of improved methods; for while the temperature of the human body was marked at 96° on the original scale, it stands at 98.6 on the scale now in use. Réaumur, a Frenchman, about 1730, found that 1000 volumes of a mixture of alcohol with $\frac{1}{5}$ water expanded to 1080 volumes between the freezing and boiling-points of water, and he marked these extremes as 0 and 80 respectively, dividing the intervening space into 80 parts. Celsius, a Swede, in 1742, proposed a scale with 0 at the boiling-point of water and 100 at the temperature of melting ice. This scale was modified and inverted by Christin, of France, and Strömer, of Sweden, independently, in 1743, and thus the present centigrade scale was introduced. It has also been claimed that the centesimal division of the thermometric scale between the freezing and boiling-points of water was first made by Linné, the famous Swedish botanist, for use in greenhouses.

When writing temperatures on the different scales, it is customary to use the abbreviations F. or Fahr. for Fahrenheit, C. or Cent. for centigrade, and R. or Réaum. for Réaumur; as, 32° F., 100° C., and 80° R. On all the scales the degrees are divided into *plus* and *minus* degrees as they may be above or below the zero point; the latter being always distinguished by the prefix of the − sign, and whenever this sign is wanting the degrees of heat are understood to be above zero; thus 18° F. would indicate 18 degrees above 0, although 14 degrees below the freezing point, etc.

Fig. 79 illustrates the relative graduation on the respective thermometric scales.

As equal spaces on the centigrade and Fahrenheit scales are divided into 100 and 180 degrees, respectively, it follows that each degree on the former scale is equal to 1.8 degrees on the latter; and since 80 degrees on the Réaumur scale equal 180 degrees on the Fahrenheit scale, each degree of the former must correspond to 2.25 degrees of the latter. Each Réaumur degree is equal to 1.25 centigrade degrees.

The following rules for the conversion of thermometric values are useful.

To convert centigrade into Fahrenheit: *Multiply by* 1.8 *and add* 32; for any number of degrees above or below the freezing-point on the centigrade scale when multiplied by 1.8 yields the corresponding number of degrees above or below the freezing point on the Fahrenheit scale.

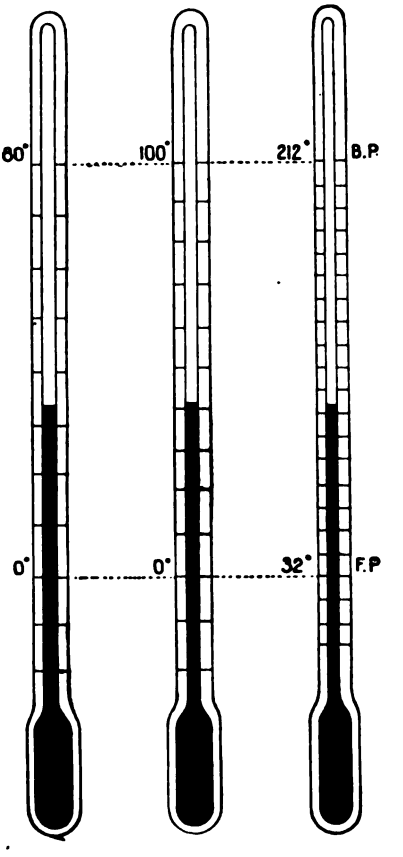


FIG. 79.—Réaumur, centigrade, and Fahrenheit thermometers.

To convert Fahrenheit into centigrade: *Subtract* 32 *and divide by* 1.8; for any number of degrees above or below the freezing point on the Fahrenheit scale when divided by 1.8 yields the corresponding number of degrees above or below the freezing-point on the centigrade scale.

To convert Réaumur into Fahrenheit, or Fahrenheit into Réaumur *substitute* 2.25 *for* 1.8 *in the preceding rules.*

To convert centigrade into Réaumur, *divide by* 1.25; and to convert Réaumur into centigrade, *multiply by* 1.25.

Examples: Convert 25° C. into F.; $25 \times 1.8 = 45$, and $45 + 32 = 77$. Answer, 77° F.
Convert −15° C. into F.; $-15 \times 1.8 = -27$, and $-27 + 32 = 5$. Answer, 5° F.
Convert −40° C. into F.; $-40 \times 1.8 = -72$, and $-72 + 32 = -40$. Answer, −40° F.
Convert 60° F. into C.; $60 - 32 = 28$, and $28 \div 1.8 = 15.55+$. Answer, 15.55 + ° C.
Convert 18° F. into C.; $18 - 32 = -14$, and $-14 \div 1.8 = -7.77+$. Answer, −7.77 + ° C.
Convert −12.5° F. into C.: $-12.5 - 32 = -44.5$, and $-44.5 \div 1.8 = -24.72+$. Answer, −24.72 + ° C.
Convert 30° R. into F.; $30 \times 2.25 = 67.5$, and $67.5 + 32 = 99.5$. Answer, 99.5° F.
Convert −5° R. into F.; $-5 \times 2.25 = -11.25$, and $-11.25 + 32 = 20.75$. Answer, 20.75° F.
Convert 50° F. into R.; $50 - 32 = 18$, and $18 \div 2.25 = 8$. Answer, 8° R.
Convert 4° F. into R.; $4 - 32 = -28$, and $-28 \div 2.25 = -12.4$. Answer, −12.4° R.
Convert 60° C. into R.; $60 \div 1.25 = 48$. Answer, 48° R.
Convert −8° C. into R.; $-8 \div 1.25 = -6.4$. Answer, −6.4° R.
Convert 28° R. into C.; $28 \times 1.25 = 35$. Answer, 35° C.
Convert −7.5° R. into C.; $-7.5 \times 1.25 = -9.37+$. Answer, −9.37 + ° C.

The Pharmacopœia gives the following description and requirements for standard thermometers intended for determination of the boiling-point and melting-point of substances: The bulbs are to be of Jena 16 III normal glass or Corning normal thermometer glass. The stems may be made of other white enamel back glass tubing having a circular cross section; the diameter of the capillary must not be greater than 0.1 mm. The diameter of the stem is to be 5.5 mm. (to within 0.3 mm.) and the maximum diameter of the bulb must not be greater than the diameter of the stem. The thermometers are to have a pear-shaped reservoir at the upper end of the capillary having a volume at least equal to the volume of the entire graduated portion of the stem.

The thermometers should be so thoroughly annealed that there will be no appreciable change in the indications after long continued exposure to the highest temperature of the scale. They should be standardized by the Bureau of Standards at Washington, and the maximum error at any temperature below 100° C. (212° F. must not exceed 0.5 nor exceed 1.0 in the interval between 100° and 350° C. (212° and 662° F.).

Thermometers reading over 200° C. (392° F.) must be filled under pressure sufficient to prevent the mercury column from boiling or breaking up into small pieces.

A set of five thermometers is recommended, all of which are to be graduated into one-half degree intervals, the length of a one degree interval being 1.5 to 2 mm. They range as follows:

Thermometer No. 1 is to be graduated from 10.5° to 125.5° C.; No. 2 is to be graduated from 98° to 225° C.; No. 2 A is to be graduated in the neighborhood of the ice point from 1° to 2°, above which is to be a small enlargement in the capillary, and then a graduated portion extending from 98° to 250.5° C.; No. 3 is to be graduated from 198° to 350.5° C.; No. 3 A is to be graduated into half degrees in the neighborhood of the ice point from —1° to +4°, above which is to

be a small enlargement in the capillary, and a graduated portion extending from 198° to 350.5° C.

As an auxiliary thermometer for emergent stem corrections, a standard thermometer from 15 to 20 cm. (6 to 8 in.) in length may be used, graduated from 20° to 100° C. into degrees.

In order to avoid the use of the ordinary long thermometer for temperatures above 100° C., which might frequently prove annoying and give rise to inaccuracies in scientific work, special short thermometers have been devised, made of Jena normal glass, and known in the trade as Anschütz thermometers. They are about 15 cm. (6 in.) long and 6 mm. (¼ in.) in diameter, and come in sets of seven, all of which are graduated in one-fifth degree intervals, and, with the exception of the lowest one, are all filled with nitrogen; they correspond practically to the official standard thermometers of the Pharmacopœia.

In pharmacy arbitrary terms are frequently employed to indicate temperatures suitable for certain operations; thus the term *gentle heat* indicates a temperature between 32° and 38° C. (90°–100° F.), and the term *moderate heat* is employed when a temperature between 45° and 50° C. (113°–122° F.) is to be used and not exceeded.

CHAPTER V.

COLLECTION AND PRESERVATION OF CRUDE DRUGS.

ALTHOUGH the collection and preparation of vegetable drugs are not in the hands of the pharmacist, but are carried on, often in a small way, by special drug-gatherers and -collectors, it is thought fit to refer to the subject here.

The various parts of plants used in medicine cannot be gathered indifferently at all seasons of the year, since the peculiar juices of the plant in which its activity resides are more abundant in some parts than others at certain periods of the plant's growth. Roots of *annual* plants should be gathered immediately before the time of flowering; those of *biennials*, either late in the fall of the first year or early in the spring of the second year, after the first appearance of the plant above ground; perennial roots should not be gathered until after two or three years' growth, and in some cases even four or five years are allowed for full maturity. Fleshy roots should be sliced, either transversely or longitudinally, previous to drying, in order to expose a larger surface to the air; while smaller and fibrous roots do not require this treatment. When artificial heat is used in drying roots, a temperature of 50° to 55° C. (about 122° to 131° F.) is sufficient, except in the case of a few succulent roots, where the temperature may be raised to 65.5° C. (150° F.).

Barks of trees should be gathered in the spring, but those of shrubs in the autumn, for at these seasons they are most readily separated from the wood. Only the inner bark being employed, the outer epidermis should be removed.

Leaves begin to lose their activity after the flowers appear, for the juices of the plant then go toward nourishing the latter; they should therefore be collected when fully developed, before they begin to wither. Leaves of biennials should be collected during the second season.

Herbs are generally understood to mean the whole plant, although the root is frequently rejected; they should be gathered when in flower. If the flowers are not to be used with the stem, the latter should be collected before the flowers appear, but after foliation.

Flowers are preferably gathered before they are perfectly developed (expanded), since odor and color are then more pronounced; the red or French rose offers a striking example. They should be collected in the morning, after the dew has disappeared, and be dried, without artificial heat, in the shade.

Fruits should be gathered before they are quite ripe; but seeds, the least perishable of vegetable productions, must be perfectly ripe, and require very little drying.

Crude vegetable drugs are rarely deprived of all their inherent moisture by the drug-gatherers, and invariably reabsorb moisture when exposed to a damp atmosphere; before such drugs can be mechanically subdivided they frequently require a further drying by artificial heat, which is effected by spreading the material loosely on perforated shelves in ventilated apartments heated by steam. While drugs containing volatile constituents, such as buchu, valerian, myrrh, spices, etc., demand a moderate heat, others again can be strongly heated until they become brittle, as, for instance, squill; a temperature kept at or below 45° C. (113° F.) will not prove injurious in any case.

The amount of moisture present in freshly gathered botanical drugs varies considerably, ranging from 15 or 20 per cent. in barks and wood to as much as 80 per cent., or more in some roots and leaves, and the object of thorough drying is partly to reduce the bulk, but chiefly to preserve the drug for future use; for if vegetable drugs be packed away in a moist condition they soon begin to mould, or become heated, and undergo rapid deterioration. The following table by Tschirch shows the average loss in weight by drying, of a number of well known drugs:

Name of drug.	Loss.	Name of drug.	Loss.
Althæa,	75 per cent.	Glycyrrhiza,	67 per cent.
Arnica flowers,	80 "	Mezereum,	50 "
Belladonna leaves,	82 "	Peppermint,	80 "
Belladonna root,	62 "	Squill,	75 "
Calamus,	75 "	Stramonium leaves,	55 "
Colchicum root,	66 "	Taraxacum,	78 "
Digitalis,	80 "	Valerian,	75 "

The loss in weight resulting from thorough drying of drugs is in many cases more than compensated for by the increase in value of the dried article, as in opium and other alkaloidal or resinous drugs. If opium containing 10 per cent. of morphine and 25 per cent. of moisture be dried perfectly, the loss in weight will amount to one-fourth, but the relative proportion of active principle is increased one-third; jalap tubers containing 8 per cent. of resin and 34 per cent. of moisture will lose upon drying about one-third of their weight, but the proportion of resin present is increased 50 per cent. Dried botanical drugs are best preserved in cool, dry rooms in containers which shall exclude sunlight, but permit of free circulation of air; odorous drugs should always be kept separate in order to avoid contamination of others; for instance, a bale of buchu, valerian, or sassafras should never be stored by the side of senna leaves, elm-bark, or flaxseed.

As crude drugs reach the pharmacist they are frequently not in a condition to be offered for sale, or to be used in the preparation

of medicines, on account of impurities present, and the process of garbling is a very necessary operation. The object of garbling, or picking, is to remove, besides impurities and adulterations, decayed and deteriorated portions of the drug, which not only mar the appearance but are apt to contaminate the still healthy portion, and soon render the whole worthless. Senna leaves are often accompanied by a considerable proportion of stems, broken capsules, and dust, not to speak of the fraudulent admixtures of stones, shells, etc., made by the gatherer or exporter for the purpose of increasing the weight; as much as 15 per cent. of impurities has been taken from what was bought as prime senna. Juniper berries are never free from unripe and decayed fruit, dirt, and worm-eaten portions, which should be carefully removed. Fibrous roots, as spigelia, wild ginger, serpentaria, and the like, require to be freed from adhering dirt and other roots that grow side by side with them, and have become mixed through careless gathering. Although some drugs are found in much better condition than others, there is none which may not be improved in appearance, even if it be only to have the fine dust and dirt removed, as in the case of sassafras, wild cherry, crushed oak bark, etc.; lycopodium, fennel, flaxseed, and similar drugs should be well shaken in a suitable sieve, to remove foreign matter, before putting them away in containers: and the careful pharmacist will find that this little extra labor is readily appreciated by his patrons, who are apt to judge a man largely by the appearance of his wares. Even vegetable powders, such as ipecac, nutgall, and others of similar character, must be passed through a fine sieve, preferably bolting cloth, to remove coarse particles which unfit them for dispensing purposes, and which have in some instances been found to amount to as much as 25 per cent. of the total weight of the powdered drug.

CHAPTER VI.

MECHANICAL SUBDIVISION OF DRUGS.

BEFORE employing vegetable drugs in the various pharmaceutical preparations, it becomes necessary to reduce them to a state of comminution, or of powder, more or less coarse or fine as the nature of the drug and the desired preparation may demand. By simple contusion is generally understood a rather coarse division, brought about by crushing or bruising in suitable apparatus preparatory to finer reduction; for small operations an iron or brass mortar of bell or urn shape is employed, which should be deep and with a broad inner base, as shown in Fig. 80, the pestle being of such length and weight as will enable the operator to exercise considerable force if necessary. In contusing substances only such a quantity should be placed in the mortar at one time as to cover the bottom for the depth of an inch or two; and to avoid loss or unpleasant results from the escape of dust or particles of drug, a cover, provided with a hole through which the pestle passes, should be used. In place of the mortar and pestle a cutting knife can frequently be used with advantage. The Champion knife No. 2, Fig. 81, made by the Enterprise Manufacturing Co., of Philadelphia, is well adapted for the coarse division of roots, barks, and herbs, as it combines a drawing motion with pressure while cutting the material. When operating on large quantities, steam power is necessary, and the best apparatus for the purpose is that known as Mead's disintegrator (see Figs. 82, 83, and 84). The grinding is done in this mill by hardened steel beaters securely riveted on both sides of a steel disk. These beaters revolve on the feeding side of the mill between corrugated rings. The beaters catch the material as it enters the mill and beat it against the corrugates until it is sufficiently fine to pass between the disk and the face of the ring; as soon as it

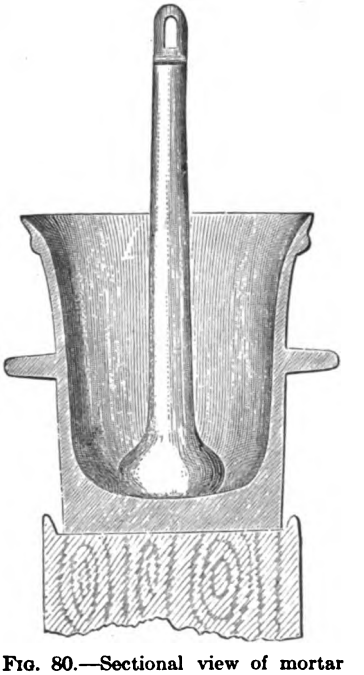


FIG. 80.—Sectional view of mortar and pestle for contusion.

passes here it is on the discharge side of the mill, and all that is sufficiently fine is immediately driven out by the beaters on the back

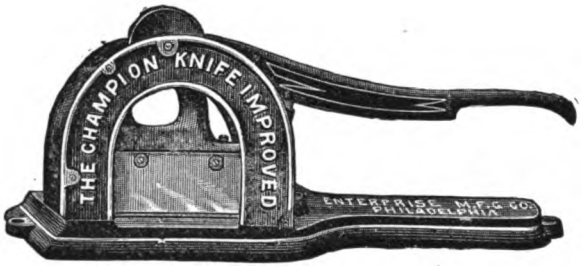


FIG. 81.—Cutter for herbs and roots.

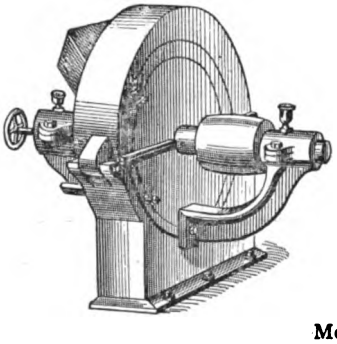


FIG. 82.—Front view.

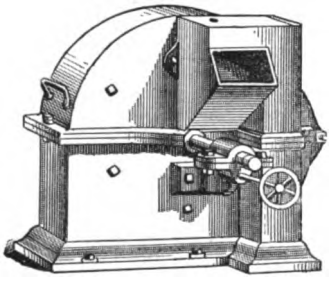


FIG. 83.—Side view.

Mead's disintegrator.

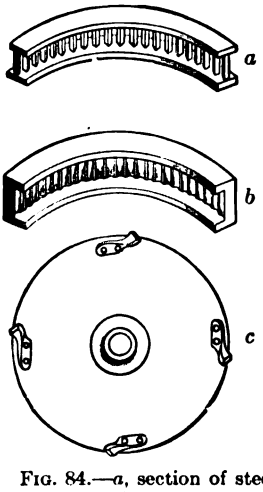
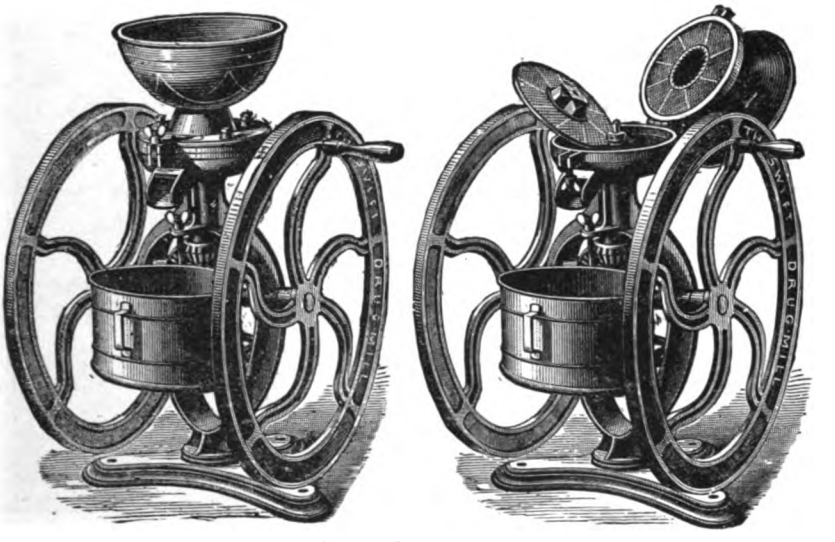


FIG. 84.—*a*, section of steel screen; *b*, section of corrugated ring; *c*, steel disk with beaters attached.

of the disk. What is not sufficiently fine to discharge is caught by these back beaters and beaten against the screens until fine enough to pass through. The screens are made of square steel, and present a grinding surface to the beaters and a discharging surface between each bar; they are 2 inches in width and extend around three-fourths of the diameter of the mill, thus giving a large discharging surface without diminishing the grinding surface. The material as it is ground falls into the box or room below. The most effective work is achieved with the disintegrator running at high speed, 3000 revolutions per minute; under such conditions 600 pounds of wild-cherry bark can be finely crushed in an hour.

The production of very fine powders of drugs has long since passed into the

hands of the drug miller, and even the coarser powders intended for percolation are today prepared by only a small number of pharmacists. For the latter purpose the drug mills shown in Figs. 85, 86, 87, and 88 will be found very desirable. In the New *B* Swift mill the grinding is done between plates placed horizontally, while in the Enterprise mill they are placed vertically. The grinding surfaces of both mills consist of circular chilled-iron castings studded with concentric rows of sharp teeth, those of one plate fitting between those of the other. The teeth decrease in size toward the center, and the fineness of the powder is regulated by a pair of screws, by means of which the plates are made to approximate each other. One of the plates is stationary while the other revolves. Separate sets



New *B* Swift mill.

FIG. 85.—The mill ready for use. FIG. 86.—The mill open.

of plates for coarse and for very fine grinding can be had for the mills. Care should be taken to clean the mill thoroughly after each operation, else the remaining dust will surely contaminate the drug next ground. The simplest method of cleaning is to run sawdust through the mill repeatedly; then loosen the screws and remove the grinding plates, so as to wash these with hot water, if necessary, and dry quickly. A great mistake often made by the inexperienced is the attempt to produce fine powders at once by screwing the plates close together, instead of grinding the drug coarsely at first and gradually tightening the mill; the first plan is apt to cause the material to become heated and cake, while the second plan will achieve the desired end more perfectly, with far less expenditure of manual labor and wear of machinery.

For grinding small quantities at the dispensing counter the No. 450 Enterprise mill (Fig. 89) is admirably adapted; it is constructed on the

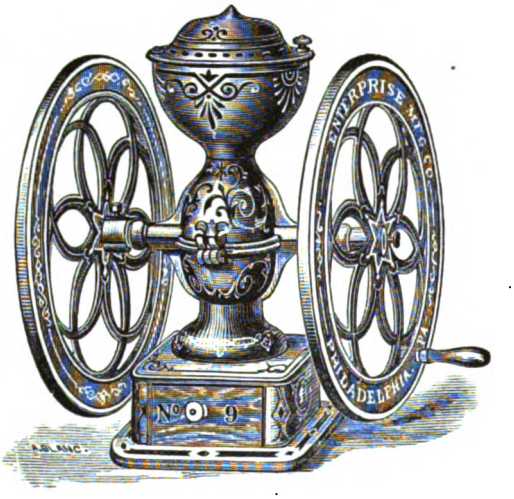


FIG. 87.—Enterprise drug mill (closed.)

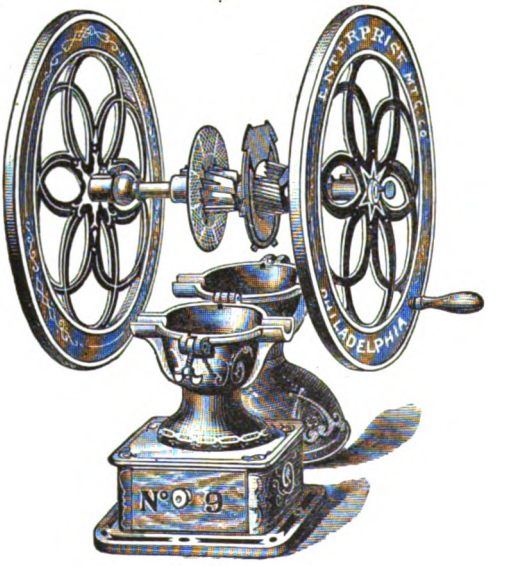


FIG. 88.—Enterprise drug mill (open.)

same principle as the larger Enterprise mill shown in Figs. 87 and 88. All the before-mentioned hand mills can be opened horizontally, as shown in the illustrations, by means of a thumb-screw and hinge;

thus the interior may be readily exposed to view for examination or cleaning. The material is supplied through a capacious hopper, with its base specially arranged for crushing the drug into coarse particles. The rapidity with which the material should be fed to the mill depends entirely upon the character of the drug, as some drugs will soften under the influence of heat and pressure, while others are not affected at all. Substances like vanilla, which cannot be heated before powdering, on account of the rapid loss of the aromatic principle, must be reduced in the soft condition; and, although the old method of grinding with sugar or clean sand is still largely in use, it is decidedly inferior to the process of cutting. Grinding or powdering vanilla has a tendency to press out the soft pulp, which soon retards the reduction of the tough fiber and requires the expenditure of much time and labor. If vanilla be reduced to the requisite degree of fineness for percolation by means of a rapid-acting cutter, it retains practically its original condition, no pulp being expressed, and a powder is obtained far superior to that by grinding with sand or sugar. Fig. 90 represents the American mince-meat chopper, an apparatus admirably adapted to the cutting of vanilla,

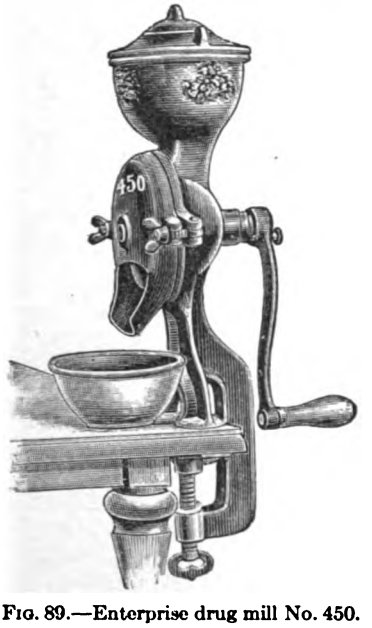


FIG. 89.—Enterprise drug mill No. 450.

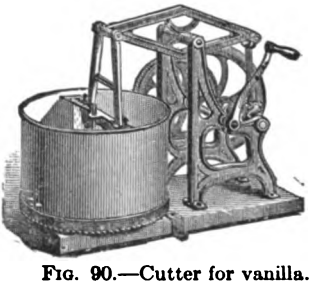


FIG. 90.—Cutter for vanilla.

and first suggested for this purpose, many years ago, by the late N. H. Jennings, of Baltimore. The large knife blade with which the cutting is effected must be kept well sharpened. As the cylinder revolves with each turn of the lever, fresh particles of the material are continually presented to the knife, and disintegration is rapidly achieved, while the aroma and virtue of the vanilla are kept intact.

The grinding of drugs on a large scale, and particularly into very fine powder, is accomplished either in buhr-stone mills, iron mills, such as the Bogardus eccentric mill, or stone "chaser" mills. In the first-named mill grinding is effected between two large stone disks placed horizontally and provided with numerous furrows to facilitate the passage of the ground drug from the center to the circumference;

one of the disks is stationary—in some mills the upper, and in others the lower—while the other revolves, the material being fed through an opening in the center of the upper stone. By suitable approximation of the stone disks, powders of various degrees of fineness can be produced.

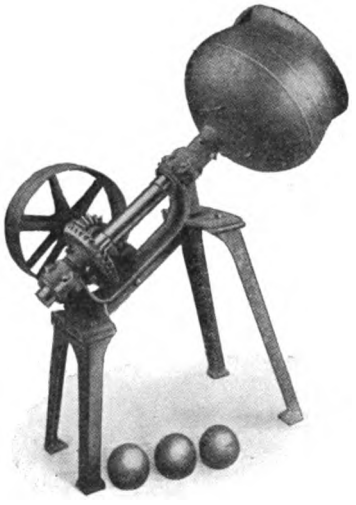


FIG. 91.—Pot mill.

Fig. 91 represents one of the smaller power mills, known as a pot mill, well adapted for grinding small quantities of drugs, which could not be reduced economically in a large mill. The grinding is accomplished by means of heavy iron balls, which crush the material as they revolve within the pot, the latter being provided with a tight cover to prevent loss of powder.

Substances liable to become heated and to cake when ground in ordinary mills, such as vegetable extracts, pepsin, etc., can be reduced to an impalpable powder in the so-called pebble or jar mills now in use by all the leading manufacturers of pharmaceutical preparations. These mills do not crush or cut the material, but grind principally by friction, the effect being produced by the sliding, tumbling, and rolling inside of porcelain or stone cylinders,

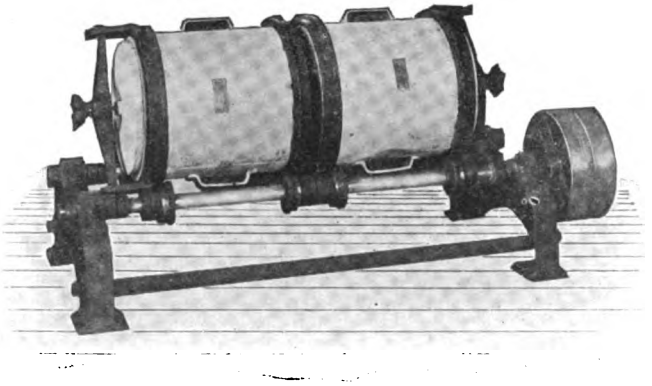


FIG. 92.—Pebble or jar mill.

encased in iron, of a large number of flint or porcelain pebbles, of about the size of large walnuts, mixed with the substance to be ground; the movement is caused by revolving the cylinder at a regu-

lated but slow rate of speed—from 25 to 50 revolutions per minute. Fig. 92 represents a pebble mill with jars made of impervious porcelain.

The portable Bogardus eccentric mill (Fig. 93) is a great favorite with drug millers, as it can be driven at a high rate of speed without becoming heated, and discharges the ground material promptly without danger of choking. Both grinding plates revolve in the same direction, on centers which are about one or two inches apart from each other, hence the name *eccentric*; this arrangement causes the material between the plates to be moved about in every conceivable manner, to be acted upon by the plates at every point, and subjected to a peculiar twisting, cutting, and grinding motion, whereby it is rapidly disintegrated, with large results in quantity ground and the expenditure of but little power. In mills with a single revolving plate (the other being stationary), one plate continually describes the same circle on the other, so that material ground in these mills is subject to motion in one direction only, hence greater power and more time are necessary to accomplish the desired result than if the material were acted upon in various directions and by different motions. The rate of feeding the mill is controlled by an adjustable slide attached to the hopper, and the degree of fineness of the powder is regulated by means of a screw and lever controlled by a weight.

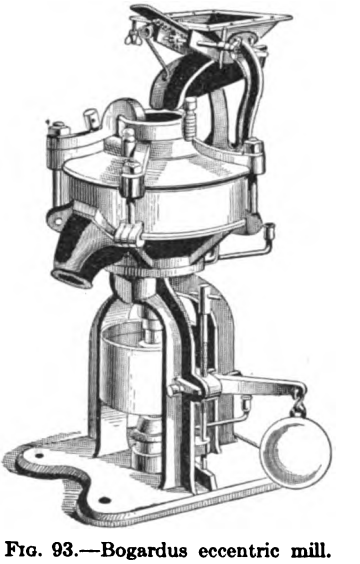


FIG. 93.—Bogardus eccentric mill.

The so-called chaser mill is preferred when large quantities of material, such as cinnamon, ginger, pepper, mustard-seed, and the like are to be reduced to impalpable powder. Fig. 94 shows a sectional view of a large chaser mill in use at the drug mills of Messrs. Gilpin, Langdon & Co., of Baltimore. It consists of two large stone disks, or granite wheels, connected by a short metallic axle with a revolving shaft, which compels them to travel in fixed lines on a base of granite. The name *chaser mill* is derived from the motion of the disks—called *chasers*—which appear to chase each other in their travels over the stone base. The grinding of any material supplied to the mill is effected between the granite base and the outer edge of the chasers; by means of iron scrapers appropriately fastened to the revolving shaft the material is continually brought under the grinding edges again. As seen in the illustration, the base is surrounded by a curb, to prevent the coarsely ground particles from mixing with the finer powder, which, by means of the draught created by the rapid revolution

of the chasers, is carried upward and over the sides of the curb. The whole mill is enclosed in a dust-proof compartment, which is frequently provided with a series of shelves for the purpose of allowing the fine particles of powder to be deposited for subsequent convenient collection. The feeding of the mill is accomplished through the top of the box, by means of a long funnel delivering the material directly upon the stone base.

Sifting.—In order to produce powder of uniform fineness, the ground substance should be subjected to the separating action of some perforated medium, whereby division into coarser and finer particles is readily effected. The construction of ordinary sieves is too well known to require special description. The perforated

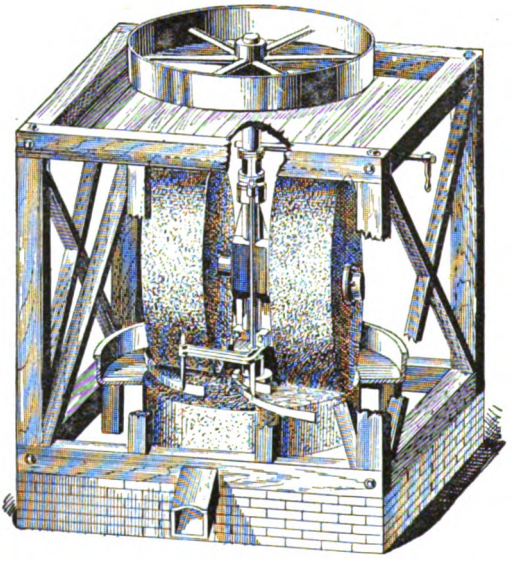


FIG. 94.—Chaser mill.

material or netting used may be made of iron, brass, or tinned wire, hair cloth for substances affected by metal, and silken cloth for very fine or dusted powders. While formerly it was customary to express the fineness of powders by numbers which represented the number of meshes per linear inch of the sieve through which the powder would pass, the particular gauge of wire being indicated in each case, the Pharmacopœia now states the fineness of powdered and granular substances in terms of the maximum diameter of the particles of powder as measured by the width of opening of the meshes of the sieves from which they receive their designating numbers.

The old sieve numbers have been retained, but now have a different meaning, thus: No. 100 powder has a fineness, in diameter of particles, less than 0.14 millimeter; No. 80 or very fine powder has a fineness,

in diameter of particles, less than 0.17 millimeter; No. -60 or fine powder has a fineness, in diameter of particles, less than 0.23 millimeter; No. 50 or moderately fine powder has a fineness, in diameter of particles, less than 0.28 millimeter; No. 40 or moderately coarse powder has a fineness, in diameter of particles, less than 0.38 millimeter; No. 30 powder has a fineness, in diameter of particles, less than 0.54 millimeter; No. 20 or coarse powder has a fineness, in diameter of particles, less than 0.85 millimeter; No. 12 very coarse powder has a fineness in diameter of particles, less than 1.47 millimeters; No. 6 powder has a fineness, in diameter of particles, less than 3 millimeters.

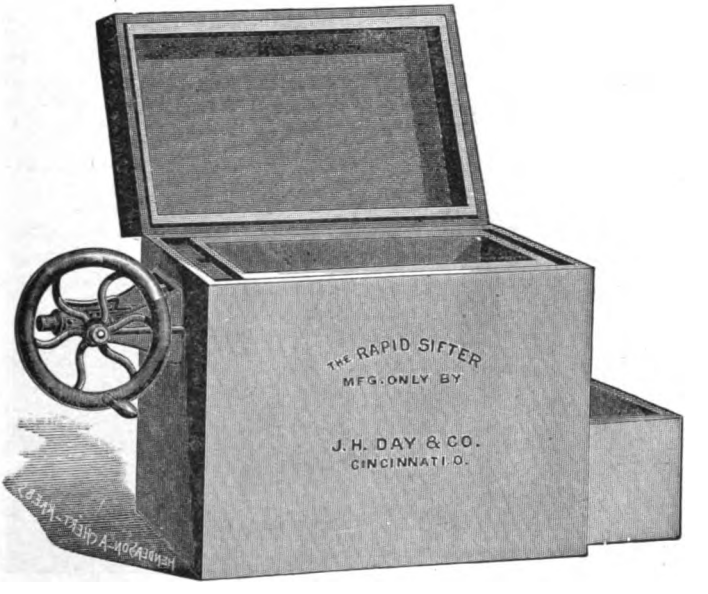


FIG. 95.—Rapid sifter.

While it is impossible to grind drugs entirely of the degree of fineness required for many purposes, the aim should be to keep the finer portion down to a low percentage by frequent sifting; a powder of a specified number must meet the requirements given above for that number of powder, but the larger proportion of it must not pass through a sieve of a lower degree of fineness. It should also be borne in mind that some parts of the drug can be ground more readily than others; it is, therefore, necessary to mix the powder thoroughly after the grinding and sifting have been completed. The proper handling of a sieve cannot be definitely described, it must be taught practically; this much, however, can be said—that no effort should be made to force the material through the meshes of the sieve by persistent pressure of the hand, which will cause the meshes to open farther and allow coarser particles to pass through. In Fig. 95 is shown an excellent

sifting machine known as the rapid sifter, which can be operated either by hand or steam power. Both wire and bolting cloth sieves can be used in this machine, in which the sifting is effected by an oscillating or shaking movement, the sifted powder being received in a drawer. It is dust-proof and made in different sizes. Of late years, sifters and mixers combined in one piece of apparatus have been preferred; such a combination, admirably adapted to the wants of the pharmacist who manufactures on a small scale, is shown in Fig. 96. Its capacity is 50 pounds, and the mixer is provided with a galvanized double spiral agitator so arranged that when the sifted powders come in contact with it the inside spiral carries the material one way, while the outside spiral carries it the other; thus a most

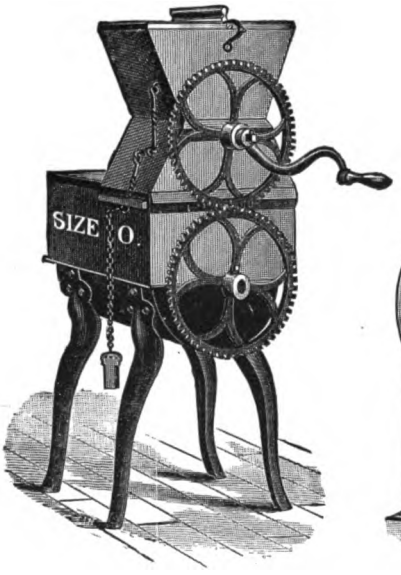


FIG. 96.—Lightning sifter.

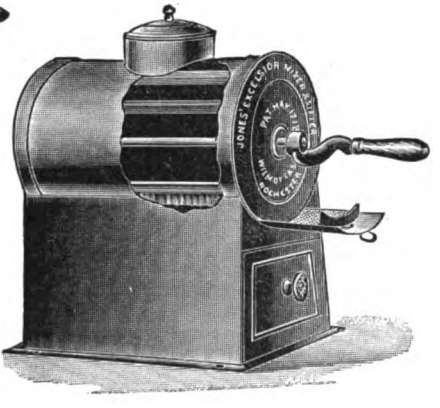


FIG. 97.—Excelsior powder mixer and sifter.

thorough mixture is effected in a short time. After the powders have been mixed, the contents may be withdrawn by means of a slide in the bottom of the circular mixer. Smaller and larger sizes of the "Lightning" sifter and mixer are manufactured, and can be supplied with sieves of different degrees of fineness. Fig. 97 represents the excelsior powder mixer and sifter, made by the F. J. Stokes Machine Company, of Philadelphia, in which the mixing is effected on a different principle, by means of paddles and brushes; its capacity is 10 pounds. These combined sifters and mixers are well adapted for the manufacture of Seidlitz mixture, tooth powder, compound licorice powder, etc., without the annoyance of dirt and dust.

Powdered drugs are frequently offered at prices lower than those

asked for a good quality of the crude drug; yet it is well known that the cost is enhanced by loss in drying and powdering, expense of grinding (from 3 to 10 cents per pound), and other incidentals. There can be but one explanation of this anomaly: either an inferior quality of drug has been ground, or admixtures have been made to increase the yield of the powder. According to Squibb, the average loss by powdering (and subsequent drying) of the following drugs has been found to be for

Acacia,	0.80 per cent.	Ginger (peeled)	9.70 per cent.
Aloes (Socotrine),	17.31 "	Ipecac,	1.91 "
Buchu,	2.00 "	Jalap,	9.58 "
Cantharides,	2.05 "	Myrrh,	5.80 "
Cardamom,	6.02 "	Opium,	19.61 "
Catechu,	1.08 "	Podophyllum,	0.75 "
Cinchona (red),	1.58 "	Rhubarb,	1.74 "
Cinchona (yellow),	2.57 "	Sarsaparilla,	0.70 "
Cinnamon (cassia),	2.61 "	Scammony,	2.70 "
Cubeb,	2.40 "	Squill,	13.60 "
Ergot,	3.62 "	Tragacanth,	6.93 "
Gentian,	10.23 "	Valerian,	1.88 "

Gilpin, Langdon & Co. of Baltimore, who carry on very extensive operations as drug millers, report the following averages of loss in grinding drugs for percolation in accordance with pharmacopœial requirements:

Aconite Root,	20 per cent.	Licorice Root,	5 per cent.
Belladonna Leaves,	23 "	Nux Vomica,	36 "
Black Haw Bark,	30 "	Orange Peel, Bitter,	26 "
Cascara Sagrada,	30 "	Rhubarb,	5 "
Chinchona Bark,	6 "	Sarsaparilla,	33 "
Calumba Bark,	30 "	Squill,	12 "
Cubebs,	6 "	Taraxacum,	25 "
Gentian,	7 "	Valerian,	35 "
Hyoscyamus,	32 "	Wild Cherry Bark,	23 "

Owing to the largely increased surface exposed to light and air in the case of powdered drugs, they are, as a rule, more liable to deterioration than crude drugs, and should therefore be more carefully protected against moisture.

Among other methods for the mechanical subdivision of drugs may be mentioned *trituration*, which consists in reduction of a substance to very fine powder by continued attrition of the particles between the hard surface of a pestle and the sides and bottom of a mortar. Trituration is usually applied to saline and similar chemical substances, and the mortars best adapted to the process are those made of Wedgwood ware, of the shape shown in Fig. 98. A rotary motion of the pestle accompanied by pressure is productive of the best results in trituration, the circles described being gradually enlarged from the center outward and back again to the center. A thin layer of the material should be kept between the pestle and the sides of the mortar. When the powder begins to cake and fall toward the center of the

mortar a spatula should be run around the sides so as to loosen up and mix the different portions. The term trituration is also sometimes employed to designate the thorough mixture of vegetable or other powders by rubbing them well together in a mortar; in such cases little if any pressure is employed, and thorough blending of the mixture is fascilitated by frequently scraping the powder from both pestle and mortar with a spatula.

The reduction of substances to fine powder by triturating them in the presence of a liquid having no solvent effect upon them is termed *levigation*. The process is usually conducted in broad, shallow mortars. Formerly, when a stone slab and muller were employed, this method was also known as porphyrization, from porphyry, a very hard stone, the material of which the slab was made. Water, alcohol, or oil may be used as a suitable medium for levigation, the process consisting of the formation of a paste of the substance to be powdered and the liquid, this paste being then triturated or ground

FIG. 98.—Wedgwood mortar and pestle.

until perfectly smooth. Red mercuric oxide may thus be reduced to an impalpable powder by trituration with alcohol; and white paints, such as zinc oxide and lead carbonate, are ground smooth with oil in special paint mills.

Elutriation is a process intended for obtaining certain inorganic substances in a finely pulverulent condition, by diffusing them in water after they have been ground or crushed; the coarser particles then rapidly subside, owing to their higher specific gravity, while the water holding the fine powder in suspension is decanted and allowed to settle in another vessel, the decantation being repeated a second time if necessary. To facilitate drying of the elutriated powder, the magma or soft mass is drained as completely as possible, and then formed into small conical nodules, which are conveniently dried on warm porous tiles. The well known soft prepared chalk, French bismuth subnitrate, and numerous lake colors, are obtained as fine powders by elutriation.

Other methods for the mechanical subdivision of drugs are *precipitation, reduction,* and *granulation.*

By *precipitation* is understood the sudden destruction of the soluble form of a substance which is held in solution; this may be effected by the addition of another substance to the solution, or by some external agency. The substance thus thrown out of solution is termed the *precipitate,* and the substance or force causing the separation—the *precipitant.* Precipitation is employed in pharmacy as a method of pulverization and purification, and as a convenient means for obtaining many insoluble substances.

The first of these comes under the head of what may be termed simple or physical precipitation, usually brought about by the addition to the solution of some substance in which the dissolved body is insoluble; as in the precipitation of ferrous sulphate or of tartar emetic from aqueous solution by means of alcohol. Other examples of physical precipitation are the separation of iodine or camphor from alcoholic solution by the addition of water, the precipitation of solution of acacia by alcohol, the precipitation of lime water by boiling, and the preparation of the official resin of jalap.

The process of precipitation when intended as a means of purification or of the preparation of insoluble compounds almost invariably involves chemical action, as in the purification of metals by electrolysis, the manufacture of mercuric iodide, etc.; in the former case simple decomposition of a salt is effected, while in the latter case mutual decomposition between two salts is necessary.

Some insoluble compounds are precipitated by simple decomposition of a substance by means of water, as bismuth subnitrate, yellow mercuric subsulphate, etc.; in the former case an acid solution is freely diluted with water, in the latter case white mercuric sulphate is thrown into boiling water.

Mercuric oxide can be obtained in a much finer state of division by precipitation than by any other method, but it must be brought about by chemical action. If a solution of mercuric chloride be poured into a solution of sodium or potassium hydroxide two new compounds, yellow mercuric oxide and sodium chloride, are formed, the latter remaining in solution, while the former separates as an impalpable powder, being insoluble in all neutral liquids. Lead iodide, magnesium carbonate, ammoniated mercury, and precipitated chalk are familiar examples of compounds prepared by chemical precipitation.

The character of the precipitate depends largely upon the conditions under which its formation is effected; thus, concentrated solutions are apt to yield dense precipitates, particularly if heat be employed, whereas cold dilute solutions, as a rule, produce light bulky precipitates. In the preparation of new chemical compounds by precipitation it is important that the proportion in which the precipitant is to be employed should be determined by calculation, as a deficiency or an

excess may result in loss from imperfect precipitation or re-solution of the precipitate. Mutual decomposition between two salts always takes place in definite molecular proportions, and the necessary quantities may be readily ascertained by writing out an equation showing the decomposition; thus the formation of yellow mercuric oxide is demonstrated by the equation $HgCl_2 + 2NaOH = HgO + 2NaCl + H_2O$, which shows that 1 molecule or 271.52 parts of mercuric chloride requires 2 molecules or 80.02 parts of sodium hydroxide for complete precipitation. In this case an excess of sodium hydroxide is not hurtful, but a deficiency would result in the production of mercuric oxychloride of brownish color instead of a pure yellow oxide. The equation $HgCl_2 + 2KI = HgI_2 + 2KCl$ shows that in the formation of red mercuric iodide 2 molecules or 332.04 parts of potassium iodide are necessary for the complete precipitation of 1 molecule or 271.52 parts of mercuric chloride; these proportions must be strictly observed, otherwise a loss will result, as red mercuric iodide is soluble in both potassium iodide and mercuric chloride solutions. When precipitation by mutual decomposition between two salts is proposed, the salts are mixed in the form of separate solutions, and perfect blending is accomplished by stirring the mixture.

The most convenient style of vessel for precipitation is a glass or stoneware jar considerably broader at the base than at the top, and provided with a lip; this greatly facilitates the subsidence of the precipitate, and the subsequent removal of the clear liquid remaining above the precipitant, known as *supernatant* liquid.

The purification of precipitates is effected by a process of washing, which consists either in mixing them repeatedly with fresh portions of water in a suitable jar, and decanting the supernatant liquid after it has become perfectly clear, or in continued affusions of water on the precipitate contained in a cloth strainer or paper filter; each portion of water should be well mixed with the precipitate and the washing continued until the complete removal of the soluble by-product has been ascertained by appropriate tests. When a precipitate tenaciously retains liquid, forming a thin paste, the mixture is termed a *magma*, and forcible expression must frequently be resorted to in order to remove the liquid, as in the case of washing ferric hydroxide, freshly precipitated calcium phosphate, etc.

The official reduced iron is an instance of a metal obtained in a finely divided state by *reduction;* ferric oxide being heated to redness in an atmosphere of hydrogen, in suitable tubes, and allowed to cool without contact of air. This method of producing metallic iron in fine powder yields better results than any other known.

Granulation is a process by which certain substances soluble in water are obtained in the form of coarse powder by simple evaporation of their solution, with constant stirring, until all moisture is dissipated. It is employed either for deliquescent and difficultly crystallizable substances, as potassium citrate and carbonate, or in cases where the

solution, if allowed to evaporate very slowly, would yield larger crystalline masses, as ammonium chloride, lead acetate, etc. Granulated powders, as the name indicates, never represent a fine state of division, but offer a very convenient form for dispensing and manufacturing purposes. Zinc and tin may be readily granulated in the metallic state by heating them to a temperature a little below their melting point, when they become very brittle, and can then be rubbed into coarse powder in a mortar.

Some substances obstinately resist pulverization by any of the methods mentioned, and require a different treatment; for instance, camphor cannot be reduced to a fine powder without being first brought to a state of partial or perfect solution by means of alcohol; a smooth paste being first formed of camphor and alcohol in a mortar; which is then triturated until perfectly dry and in the form of an impalpable powder; excessive pressure should be avoided during the trituration. Powdered camphor thus prepared is prone to return gradually to a crystalline condition no matter how carefully it is preserved, but this can be prevented by precipitating the camphor in the presence of some powder with which it will become intimately mixed. Such a process was first published in Parrish's *Treatise on Pharmacy*, and is as follows: 4 ounces of camphor dissolved in 8 fluidounces of alcohol are poured slowly, with constant stirring, into a smooth mixture of 16 grains of calcined magnesia and 2 pints of water; the precipitated camphor, enveloping the magnesia, soon rises to the surface, and is removed by pouring the whole mixture on a paper filter, where it is allowed to drain. To facilitate drying of the mass, it is cut with a spatula into small particles, and is finally preserved in bottles. Although retaining a very small amount of moisture, this precipitated camphor keeps excellently, and may be used for all purposes requiring camphor, except cases of solution. Iodoform and boric acid can also be quickly reduced to an impalpable powder by trituration with alcohol, whereby partial solution is effected, and a dry powder is obtained upon evaporation of the alcohol. Friable substances, which are not held together by strong cohesive force, but the particles of which are likely to cake when submitted to pressure, may be powdered by simple friction over a perforated surface; no better method is known for obtaining magnesium carbonate in an impalpable condition than by rubbing the cakes over the surface of an inverted bolting cloth sieve.

CHAPTER VII.

SOLUTION.

WHEN a solid body is brought into contact with a liquid in such an intimate manner that it loses its original form and assumes that of the liquid, producing a clear and uniform fluid, the process is termed solution, as is also the newly formed homogeneous liquid. The process of solution, however, is by no means restricted to the liquefaction of solids by fluids, as gaseous and liquid substances can also be brought to the condition of perfect molecular blending characteristic of solution; examples: glycerin and water, alcohol and water, castor oil and alcohol, olive oil and chloroform or ether, Peru balsam and alcohol, chlorine gas and water, ammonia gas and alcohol or water. Some solid substances when brought into intimate contact by trituration with certain other solids also produce clear, uniform liquids, and such interaction is termed solution, as in case of camphor and hydrated chloral, camphor and salol, or camphor and thymol. The fluid used to produce solution is called a solvent or menstruum, the latter name being derived from the Latin *menstruus*, meaning monthly (from *mensis*, a month), and was applied because of some influence which the changes of the moon, and consequently the time of the month, was supposed to exert upon the preparation of solvents. The view at present held by scientists regarding the electrochemical decomposition of bodies in a state of solution need not be considered here; by some the process of solution is looked upon as one of great force and activity, and this view may in the course of time clear up many hitherto unexplained phenomena.

Two kinds of solution are recognized in pharmacy, namely, *simple* and *complex* solution; in the former the solvent produces no change in the sensible characteristics of the dissolved body, simply altering its physical condition, while in the latter, where solution takes place as the result of chemical action, the properties of both the solvent and the dissolved body become modified by the loss of old or the acquisition of new properties. In the case of a simple solution, the taste, odor, color, and chemical properties of the dissolved body remain intact and are imparted to the solution; as, for instance, solutions of sugar, table-salt, or potassium permanganate in water. In simple solutions the dissolved body can be recovered in its original condition by evaporation of the solvent. Complex solutions should not be confounded with compound solutions; the latter term indicates a mixture of solutions which may all be simple in character, while complex solutions are understood to be the result of chemical action, and are accompanied

by one or more of the following phenomena: heat, effervescence, change of color, odor, and taste; as, for example, the solution of a Seidlitz powder or the solution of red mercuric oxide in nitric acid. The products obtained by evaporation of a complex solution will be found to have properties not possessed originally by the solvent or the dissolved body.

The greater the extent of surface exposed by the solid body to the liquefying action of the solvent, the more rapidly will solution be effected; hence mechanical division facilitates solution, because the latter process is in direct opposition to cohesion. A simple solution of solid substances may be considered as a fluid produced by the intimate union of the solvent and the dissolved body in a state of minute division, the union and division being so complete that the forces of cohesion and gravity are suspended, otherwise a mixture only is produced, and the solid substance will again separate. The agitation of a mixture of a solid substance and solvent also causes more rapid solution, by constantly bringing fresh portions of the fluid into contact with the solid; if equal weights of acacia or sugar, in lumps or in fine powder, be placed in separate vessels with a sufficient quantity of water, the one being actively stirred while the other is allowed to remain at rest, solution will be completed in the former vessel long before it occurs in the latter; this is due to the fact that in the second vessel a dense solution will form immediately around the solid particles, and thus prevent the remainder of the fluid from exerting its solvent action.

The simplest way of effecting solution of solids is to bring them in the form of powder into contact with the solvent in such a way that frequent agitation of the mixture is possible; for saline and similar substances a porcelain or Wedgwood mortar, which admits of active trituration, is best adapted. Considerable saving of time may be effected in the solution of larger quantities of solids, if the powdered substance be repeatedly triturated with fresh portions of the solvent, each portion of solution being poured off when saturated. Small quantities of readily soluble substances, such as potassium iodide and bromide, silver nitrate, zinc sulphate, and the like, may be placed directly in a bottle with the solvent, and the mixture agitated until perfect solution results. Some substances, of hygroscopic or deliquescent character, are preferably not reduced to powder before adding the solvent, in order to avoid agglutination; such are the official scale salts of iron, which will dissolve more speedily if shaken with water in scale form than in fine powder. Whenever heat must be employed for small operations of solution, a glass flask will be found more desirable than a dish, as evaporation of the solvent will thus be materially retarded. Solutions of solids are known to be denser than the solvent used in preparing them, and advantage is frequently taken of this fact to facilitate the solution of large quantities of solid substances, or of such as are liable to form viscid solutions, or, where stir-

ring or agitation is impracticable, by what is commonly known as *circulatory displacement*, which consists in suspending the soluble matter just below the surface of the solvent, either on a porous diaphragm, in a bag of loosely textured cloth, or in a perforated vessel, which should be moved about from time to time. By this arrangement, that portion of the solvent least charged with soluble matter is always in contact with the solid, and as the solution becomes saturated it sinks to the bottom, displacing the portion less charged with the solid, which rises to the surface, and thus a continual circulation or system of currents, favorable to rapid solution, is kept up in the fluid.

Heat, as a rule, favors the solution of solids and diminishes the solubility of gases, but there are no substances totally insoluble in the cold which become soluble by the aid of increased temperature. The effect of the application of heat is the establishment of currents in the liquid which facilitate solution, just as agitation of the vessel favors the same result; and moreover, since heat intensifies molecular motion in both the menstruum and the solid, not only will an increased quantity of the latter assume the fluid state, but solution will also be effected in less time, on account of the energetic intramolecular activity. There are some exceptions to the general rule that heat increases the solubility of substances; for instance, common salt is about as soluble at ordinary temperatures as at the boiling point of water; sodium sulphate, or Glauber's salt, increases in solubility rapidly from 15° C. (59° F.) to 34° C. (93.2° F.), at which point water takes up 4 times its weight of the salt, but beyond this temperature its solubility again decreases until 100° C. (212° F.) is reached, when water takes up about 2.13 times its weight of the salt; calcium citrate and sulphate as well as slaked lime are far less soluble in hot water than in cold, and will be readily deposited if their solutions be boiled.

The term "solubility," when no solvent is mentioned, always refers to the behavior of the substance toward water at the ordinary temperature—about 15.6° C. (60° F.); thus the statements that sugar is soluble and bismuth subnitrate is insoluble refer solely to the liquefying effect which water has upon the two substances. Different degrees of solubility are expressed by such terms as *sparingly soluble, soluble,* and *very soluble;* these varying degrees of solubility do not determine the rapidity of solution, for some substances are known to dissolve slowly but to a greater extent than others which enter into solution more rapidly but in less proportion. Substances differ greatly in their solubility in water; as extremes may be mentioned zinc chloride, soluble in one-third of its weight of water, and barium sulphate, which requires about 800,000 times its weight of water for solution. Substances but slightly soluble in water may be very soluble in other liquids; as camphor, which requires about 1000 parts of water for solution, but is readily soluble in one-third of its weight of chloroform.

The Pharmacopœia, in the case of nearly every soluble substance,

indicates the degree of solubility by stating the number of milliliters (or cubic centimeters) of water necessary to dissolve 1 Gm. of the substance, and in the majority of cases also the number of milliliters (or cubic centimeters) of certain organic solvents, such as alcohol, ether, chloroform, glycerin, etc., necessary for solution of 1 Gm. of the substance. These proportions are given for a temperature of 25° C. (77° F.) and in some cases also for water and alcohol at higher temperatures.

Since the presence of impurities influences the solubility of a substance, substances to be tested should conform at least to the purity requirements of the Pharmacopœia, as should also the solvents. Other very essential requisites for the determination of solubilities are the maintenance of a constant temperature during the course of the determination, the complete saturation of the solution and accurate analysis of the saturated solution. For the determination of solubility in water, the simplest apparatus is a thick-walled test tube of about 20 mil. (or Cc.) capacity and provided with a well washed rubber stopper; for organic solvents, however, glass-stoppered cylinders should be used. Some of the solvent having been poured into the tube or cylinder, a quantity of the finely powdered substance to be tested, sufficient to insure an excess, is added, the stopper inserted and the whole placed upright in a waterbath kept at 25° C. (77° F.) by means of a thermoregulator, the tube or cylinder being preferably kept in constant but slow rotation by means of some mechanical device, or being shaken frequently by hand, during the continuance of the bath immersion, which should last for several (eight or ten) hours to insure complete saturation. After the excess of the powdered substance has been allowed to settle, a portion of the clear solution is withdrawn and transferred to a tared glass or platinum dish, and then weighed. If the solution is not clear above the settled powder, filtration must be resorted to, either through paper or a pledget of cotton. After evaporation of the clear solution to dryness on a waterbath, the residue is weighed and from this weight the ratio of solubility can be readily calculated. Thus if the clear solution weighed 12.5 Gms. and the residue 2.5 Gms., the solvent present must have weighed 10 Gms., and $10 \div 2.5 = 4$, showing that 1 part of the substance is soluble in 4 parts of the solvent. Where greater accuracy is required, the mixture of substance and solvent left after withdrawal of the first portion of the clear solution, should be continued in the constant temperature waterbath with constant rotation or frequent agitation for two or three hours more, and then another analysis of the solution made; the results of the two determinations should agree, showing that in both cases a saturated solution was analyzed.

The determination of the solubility of a substance at temperatures above the normal becomes more difficult on account of the loss incurred during the filtration of hot liquids by ordinary methods. The late Dr. Charles Rice devised a very useful and simple apparatus,

called by him a lysimeter (from the Greek λύσις, solution), which enables the operator to obtain a clear filtrate without any loss whatever, even at the boiling temperature of liquids. Fig. 99 shows the construction of the lysimeter, which consists of a glass tube, *a*, 15 centimeters (6 inches) in length and 1 centimeter ($\frac{2}{5}$ inch) in external diameter, provided at one end with a well ground stopper, *c*, while the other end is cup-shaped, there being a contracted neck between the cup and the main tube. Into this cup is made to fit a carefully ground glass bell, *e*, having a small perforation in its bottom, as shown in *f;* there is also a stopper, *b*, which is carefully ground to fit into the cup, and which is inserted after the glass bell, *e*, has been removed.

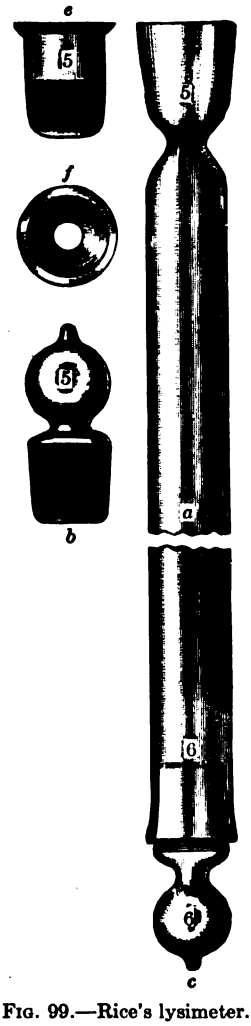


FIG. 99.—Rice's lysimeter.

When using the apparatus it is necessary to provide sufficient liquid to allow at least one-half of the tube, *a*, to be immersed; beaker glasses, or preferably wide test tubes, may be used for effecting the solution. Suppose it is desired to ascertain the solubility of a substance in boiling alcohol. The following is the plan of procedure: Insert the stopper *c* into the tube *a*, and into the cup-shaped end insert the glass bell *e*, containing a pledget of purified cotton, and secured in place by a thin platinum wire passing around the contracted neck and over the mouth of the bell. Sufficient alcohol having been put into a wide test tube or a beaker, the same is heated in a waterbath and the finely powdered substance added until, after boiling has continued for some time, a portion of the substance remains undissolved. The lysimeter, prepared as above directed, is now inserted into the liquid, and when the tube has assumed the temperature of the boiling liquid the stopper *c* is removed, which enables the solution to filter through the pledget of cotton and rise in the tube as far as the quantity of fluid will permit. If the filtered solution be allowed to flow back through the cotton once or twice, greater uniformity of the liquid will be insured. The stopper *c* is now reinserted, the apparatus withdrawn from the liquid and turned upside down to allow the bell *e* to be removed and the stopper *c* to be inserted in its place. The stoppered tube is carefully cleaned externally by washing with alcohol, and laid aside until cold. The tare of the stoppered tube having previously

been ascertained, the increase in weight must represent the weight of the solution contained therein. After transferring the solution to a tared capsule or beaker the tube is carefully rinsed with alcohol, and the washings added to the contents of the capsule or beaker; the solution is slowly evaporated on a waterbath, and afterward heated to dryness in a drying oven, when the weight of the residue will indicate the weight of the dissolved substance, and subtracting this from the weight of the solution gives the weight of alcohol. From these data the ratio of solubility is calculated in the manner already explained in the example given for determining the solubility at normal temperature.

Rapid simple solution of solid bodies is always accompanied by a fall in temperature, while a solution of gases causes a rise in temperature; these phenomena are in accordance with the laws governing the state of aggregation of bodies. Solids, for the assumption of the fluid state, require a certain amount of energy or heat, which is withdrawn from the surrounding liquid and becomes latent, while gases when condensing to liquids give out an amount of heat corresponding to that required for maintenance of the gaseous state. Four ounces of ammonium nitrate or potassium iodide rapidly shaken in a bottle with two ounces of pure water will produce sufficient cold to condense the moisture of the air on the outside of the bottle and freeze it into a thin coating of ice.

Since rapid simple solution causes a decided fall in temperature, advantage is taken of the fact that some substances hasten the liquefaction of others in the production of so-called freezing mixtures; thus, 5 parts each of ammonium chloride and potassium nitrate dissolved in 19 parts of water will cause a drop of temperature of 20° C. (36° F.); a mixture of 2 parts of snow and 3 parts of crystallized calcium chloride will cause the temperature to fall from 0° C. (32° F.) to —45.5° C. (—50° F.) and freeze mercury; the usual mixture for ice-cream freezers consists of salt with twice its weight of snow or crushed ice, which produces a temperature equal to about —20° C. (—4° F.), the cream in the cylinder freezing by reason of the great abstraction of heat necessary for the rapid liquefaction of the ice and snow surrounding it—not, as some persons believe, because intense cold is imparted to it from the outside.

Salts which have been deprived of their water of crystallization, and thus been converted into anhydrous amorphous powders, will cause a more or less marked rise in temperature when brought into solution; the heat thus generated must be looked upon as due to chemical action involving the restoration of water necessary for the assumption of the crystallized state by the anhydrous salt. If crystallized sodium carbonate be shaken with twice its weight of water, a marked fall in temperature will be noticed, whereas anhydrous sodium carbonate shaken with twice its weight of water causes a rise in temperature, thus proving the correctness of the preceding

supposition. When liquids are dissolved in other liquids no change of temperature will occur in the mixture unless contraction of volume takes place, as in the case of alcohol and water or sulphuric acid and water.

Saturated Solutions.—Saturated solutions in a pharmaceutical sense, are such as cannot take up any more of the dissolved body at ordinary temperature; in other words, the solvent has become charged with as much soluble matter as it is capable of retaining in intimate union at the ordinary temperature. The statements of ratio of solubility in the Pharmacopœia and elsewhere always refer to the formation of saturated solutions at the temperature named; thus the statement that cane sugar is soluble at 25° C. (77° F.) in 0.46 part of water and 137.2 parts of alcohol, in $\frac{1}{6}$ part of boiling water and 28 parts of boiling alcohol, means that with the proportions of water and alcohol named sugar forms saturated solutions at the temperatures indicated. Supersaturated solutions are those in which the solvent, by artificial means, has been made to take up more of the soluble matter than it is capable of retaining under ordinary circumstances; they are very unstable and present a peculiar condition of solubility. If 3 parts of sodium sulphate be dissolved in 1 part of water at 30° C. (86° F.), the solution carefully filtered into a perfectly clean dry bottle free from dust, and allowed to cool gradually, it will remain clear as long as it is not disturbed, although supersaturated, since water at 15° C. (59° F.) can dissolve only about one-third of its weight of the salt; but if the bottle containing the supersaturated solution be shaken, or a little broken glass be introduced, the whole contents will suddenly congeal to a crystalline mass. Saturated solutions of salts are frequently capable of dissolving other salts, and thus may be used for purposes of purification; if potassium nitrate be treated with a saturated aqueous solution of the same salt, no more potassium nitrate can be taken up, but impurities present will enter into solution and may be thus removed.

The effect which the presence of one substance may have upon the solubility of another is interesting as well as of practical value in pharmacy. Corrosive sublimate is far more soluble in water in the presence of alkali chlorides, and red mercuric iodide is readily dissolved in a solution of potassium iodide; in both cases union takes place between the mercuric and alkali salts. The increased solubility of potassium chlorate in the presence of sodium bicarbonate is well known; mutual decomposition, no doubt, results, the newly formed salts, sodium chlorate and potassium bicarbonate, requiring only 1.1 part and 3.2 parts of water at 15° C. (59° F.) respectively for solution, as against 16.7 and 12 parts for the original salts. Ordinarily iodine requires about 3000 parts of water for solution, but if mixed with twice its weight of potassium iodide it will readily dissolve in 20 times its weight of water. In this case no chemical union takes place, as the iodine has every apperance of being dissolved but not combined; it

retains its characteristic color and odor, and if the solution be boiled in a test tube the iodine can be completely volatilized, a portion subliming in the cooler part of the tube in its original condition.

A marked example of the effect of the presence of one substance on the solubility of another is found in the well known compound solution of sodium phosphate, largely used by physicians. Sodium phosphate contains ordinarily about 60 per cent. of water of crystallization, and is soluble at 15° C. (59° F.) in 6 pars of water; if 100 Gms. of the salt be triturated with 13 Gms. of citric acid and 2 Gms. of sodium nitrate until liquefied, and enough water then added to bring the volume up to 100 mils. (or Cc.) the solution will keep. This solution, which represents about 60 grains of sodium phosphate in each fluidrachm, is the result of chemical action, and is called by some solution of sodium citrophosphate.

In striking contrast to the above examples may be mentioned the insolubility of potassium sulphate in a solution of ammonium sulphate and of potassium nitrate in a solution of ammonium nitrate.

Solutions of solids always measure more than the liquid used to prepare them, but never as much as the combined volumes of the solvent and dissolved body. The increase in volume will naturally vary considerably, and be greatest when the substance to be dissolved is very soluble, as sugar, sodium salicylate, or potassium iodide in water. Another factor determining the volume of the solution is the presence of large proportions of water of crystallization. The following table of saturated solutions, prepared at the temperature of 15° C. (59° F.), is of interest.

Name of Substance.	Quantity of Substance Used.	Quantity of Water Used.	Volume of Finished Solution.
Borax,	6 Gms.	96 Cc.	99 Cc.
Ferrous Sulphate,	40 "	72 "	93 "
Magnesium Sulphate,	40 "	60 "	82 "
Potassium Bromide,	40 "	64 "	77 "
Potassium Chlorate,	5 "	85 "	87 "
Potassium Iodide,	40 "	30 "	42 "
Sodium Bicarbonate,	6 "	68 "	71 "
Sodium Chloride,	20 "	56 "	63 "
Sodium Phosphate,	12 "	72 "	79 "
Sodium Salicylate,	40 "	36 "	61 "
Sodium Sulphate,	20 "	56 "	69 "
Sugar,	60 "	30 "	68 "

(Borax, ferrous sulphate, magnesium sulphate, sodium phosphate, and sodium sulphate contain water of crystallization varying from 45.31 per cent. to 60.3 per cent. of the weight of the substance.)

Percentage Solutions.—This term is applied to solutions of definite strength, containing a specified amount of soluble matter in 100 parts of the solution; thus a 1 per cent. solution is composed of 1 part of the soluble substance and 99 parts of the solvent; or a 5 per cent. solution is composed of 5 parts of the soluble substance and 95 parts of the solvent, etc. For solids and gases percentage solutions should

always be prepared by weight, while for liquid substances either weight or volume may be employed. The quantity of soluble substance and solvent necessary to make a specified quantity of any particular percentage solution may be readily ascertained by the following rule: *Multiply the quantity of solution desired, in grams or grains, by the number expressing the percentage, divide the product by* 100, *and the quotient will indicate the quantity of soluble substance necessary; subtract this from the total quantity of solution desired, and the remainder will indicate the necessary quantity of solvent.*

Examples: Wanted 500 Gms. of 10 per cent. carbolized oil: 500 × 10 = 5000, and 5000 ÷ 100 = 50; 500 — 50 = 450. Answer: Dissolve 50 Gms. of crystallized carbolic acid in 450 Gms. of olive oil.

Wanted 750 grains of 4 per cent. cocaine hydrochloride solution: 750 × 4 = 3000, and 3000 ÷ 100 = 30; 750 — 30 = 720. Answer: Dissolve 30 grains of cocaine hydrochloride in 720 grains of distilled water.

Wanted 640 Gms. of 2 per cent. mercuric chloride solution: 640 × 2 = 1280, and 1280 ÷ 100 = 12.8; 640 — 12.8 = 6272. Answer: 12.8 Gms. of mercuric chloride must be dissolved in 627.2 Gms. of distilled water.

Wanted 480 grains of 20 per cent. quinine oleate: 480 × 20 = 9600, and 9600 ÷ 100 = 96; 480 — 96 = 384. Answer: Dissolve 96 grains of quinine alkaloid in 384 grains of oleic acid.

Sometimes a percentage solution of two or three substances is wanted; in such a case the absolute quantity of each active ingredient is first ascertained by the rule given above; the sum of their weights is then subtracted from the total quantity of solution desired to find the necessary weight of the solvent; for instance: Wanted 250 grains of 8 per cent. cocaine hydrochloride solution, containing also 2 per cent. of boric acid: 250 × 8 = 2000, and 2000 ÷ 100 = 20; 250 × 2 = 500, and 500 ÷ 100 = 5; 20 + 5 = 25; 250 — 25 = 225. Answer: Dissolve 20 grains of cocaine hydrochloride and 5 grains of boric acid in 225 grains of distilled water.

When a definite volume of a weight percentage solution is wanted, the quantity nearest in volume to that required must be made; although this sometimes involves a slight loss, there is no other method known if accuracy is to be preserved. Thus, if 2 fluidrachms of a 4 per cent. solution of any soluble chemical are wanted, 5 grains of the substance must be dissolved in 120 grains of water; the 125 grains of solution will measure a trifle more than 2 fluidrachms. If 8 fluidounces of a 10 per cent. solution are wanted, 4000 grains of solution must be made by using 400 grains of the medicinal agent and 3600 grains of water; 8 fluidounces of water weigh 3646 grains, hence the excess of solution will not be large. If a quart of 1 per cent. mercuric chloride solution is desired, 15,000 grains of solution must be made, as the weight of a quart of water is 14,583 grains, which is only 267 grains less than the quantity of water necessary; 150 grains of mercuric

chloride dissolved in 14,850 grains of water yield only a little over ½ fluidounce more of the solution than is wanted. If 500 mils. (or Cc.) of a 5 per cent. solution are desired, 520 Gms. of the solution must be made, the excess of solution being slight, for 5 per cent. of 520 Gms. is 26 Gms., thus allowing the use of 494 Gms. of water. When solvents other than water are used, having a higher or lower specific gravity, due allowance must be made for this fact, as the volume of a liquid compared with that of an equal weight of water varies with the specific gravity of the liquid; thus, if 4 fluidounces of a 5 per cent. solution of iodoform in alcohol are desired, it will suffice to make 1600 grains, of which 80 grains must be iodoform and 1520 grains alcohol; this will insure the full volume desired, as the specific gravity of official alcohol is 0.820, and 4 fluidounces will therefore weight only 1494.7 grains (for $455.7 \times 4 \times 0.820 = 1494.69$), whereas 4 fluidounces of water weigh 1822.8 grains. If a definite volume of a percentage solution in glycerin is required, it becomes necessary to make a larger quantity by weight than for the same volume of an aqueous solution, because the specific gravity of glycerin is 1.25, or one-fourth higher than that of water, while its specific volume is only 0.8, or one-fifth lower than that of water. To make 250 mils. (or Cc.) of a 10 per cent. solution of borax in glycerin would require 35 Gms. of borax and 315 Gms. of glycerin, yielding 350 Gms. of solution; this quantity will not be much in excess of 250 mils. (or Cc.), since the volume of 315 Gms. of glycerin is 252 mils. (or Cc.) ($315 \div 1.25$), and the presence of the borax will not very materially increase the volume. When strong percentage solutions of saline substances are made the latter often increase the volume of fluid markedly, and particularly so if they contain much water of crystallization, as shown in the table on page 133.

Solutions of arbitrary strengths are frequently employed, and although not as accurately made as percentage solutions, nevertheless seem to answer the purposes well for which they are intended. They are usuall prepared as follows:

Strength of solution.	Quantity of soluble substance used.	Quantity of water used.
1 in 250	1 grain	4½ fluidrachms.
	1 gram	250 milliliters.
1 in 500	1 grain	9 fluidrachms.
	1 gram	500 milliliters.
1 in 1000	1 grain	18 fluidrachms.
	1 gram	1000 milliliters.
1 in 5000	1 grain	11 fluidounces.
	1 gram	5 liters.
1 in 10,000	1 grain	22 fluidounces.
	1 gram	10 liters.
1 in 50,000	1 grain	110 fluidounces.
	1 gram	50 liters.

(It is evident that if metric weights and measures are used, much greater accuracy will be insured.)

Sometimes physicians prescribe solutions to be made of such strength that a tea- or a tablespoonful added to sufficient water to make either

a pint or a quart of liquid, shall represent some definite strength, such as $\frac{1}{10}$ per cent., 1 per cent., 2 per cent., 1 in 1000, 1 in 5000, 1 in 10,000, etc. Such solutions may be made as follows: Calculate how much of the medicinal substance must be in the total volume of diluted liquid in order to represent the desired strength; then calculate the number of tea- or tablespoonfuls in the quantity of solution prescribed and multiply this number by the quantity, grains or grams, of medicinal substance found necessary for the total volume of diluted liquid. Finally, dissolve the medicinal substance in sufficient water to make the prescribed volume of the stronger solution. For example:

Wanted 8 fluidounces of a solution of mercuric chloride of such strength that a tablespoonful diluted with water to one quart shall represent a $\frac{1}{10}$ per cent. solution. A quart of water weighs 14,582.4 (practically 14,600) grains, and $\frac{1}{10}$ per cent. of 14,600 is 14.6; hence each tablespoonful of the solution prescribed must contain 14.6 grains of mercuric chloride. As there are 16 tablespoonfuls in 8 fluidounces, 16 times 14.6 grains, or 233.6 (practically 234) grains of mercuric chloride should be dissolved in sufficient warm distilled water to make 8 fluidounces of solution when cold. As $\frac{1}{10}$ per cent. represents $\frac{1}{1000}$ of the whole, this solution diluted as above also represents a 1 in 1000 strength. (It may be argued that the percentage composition of the diluted solution is not absolutely correct, but the difference is extremely slight and the actual strength is as near $\frac{1}{10}$ per cent. as it is possible to get under the circumstances.)

Wanted 4 fluidounces of a solution of silver nitrate of such strength that one teasponful diluted to a pint shall represent a solution containing 4 grains of the silver salt to the fluidounce. As a pint contains 16 fluidounces, the dilution must represent 16 times 4 grains, or 64 grains of silver nitrate, and this quantity must be present in each teaspoonful of the strong solution. There are 32 teaspoonfuls in 4 fluidounces, and hence 32 times 64, or 2048, grains of silver nitrate must be dissolved in sufficient distilled water to produce 4 fluidounces of solution.

Wanted a solution of sodium chloride of such strength that 50 mils. (or Cc.) diluted to one liter shall represent physiological or normal salt solution. The latter contains 8.5 Gms. of sodium chloride in 1000 mils. (or Cc.). Every 50 mils. (or Cc.) of the stronger solution to be made must, therefore, contain 8.5 Gms. of sodium chloride, and the solution must invariably be made with sterilized distilled water.

Colloidal Solutions.[1]—While the subject of colloidal solutions belongs more properly to the field of physical chemistry, it is nevertheless of considerable interest in pharmacy, as serving to explain many conditions and phenomena, such as the formation of emulsions, the nonprecipitation of certain chemicals, etc. Strictly speaking, colloidal

[1] More complete information concerning colloidal solutions may be found in a most interesting book by W. Ostwald, entitled Colloid Chemistry, an English translation of which, by Martin H. Fischer, has been published by P. Blakiston's Son & Co.

solutions can not be considered as true solutions, although they appear as clear homogeneous liquids which pass through filter paper and do not separate by sedimentation, and must be looked upon rather as suspensions of invisible minutely divided particles, which are capable of being detected by means of a special apparatus, such as the ultramicroscope, so constructed that with high power lenses aided by very strong light concentration, the particles become visible.

By means of strong electric currents sparking under water between poles of the respective metals, copper, gold, mercury and silver have been disintegrated and the particles obtained in colloidal form, being apparently in solution, but actually in invisible suspension, and giving rise to liquids of various colors, such as blue, pink, red or violet. Such colloidal solutions are mainly of scientific interest and are rather sensitive to change, being often destroyed by introduction of other matter, such as particles of dust, foreign salts, etc.; yet when carefully preserved, they have been known to retain their original condition for many months. They are also known to be more permanent in the presence of normal colloids, such as acacia, albumen, gelatin, etc., which seem to serve as protective agents by forming films around the colloidal particles.

It has been observed that in many cases the particles of colloidal matter carry electrical charges, due possibly to partial ionization of the substance, and furthermore that such electrified particles are precipitated by addition of electrolytes to the colloidal suspension, while non-electrified colloids are not so affected.

Liquids as well as solids are capable of furnishing colloidal solutions, the name "emulsoids" being applied to the former and the name "suspensoids" to the latter. Colloidal solutions are not necessarily confined to water as a vehicle, alcoholic, ethereal and oily solutions also having been obtained. In the case of the metals of the alkalies and alkaline earths, which decompose water, colloidal ethereal solutions variously colored, have been made.

Colloidal solutions of substances ordinarily insoluble in water may also be obtained by chemical means, thus: If a solution of 0.015 Gm. of crystalline gold chloride and 0.6 Gm. of potassium bicarbonate in 125 mils. (or Cc.) of purest distilled water be boiled and a trace (about 0.01 mil. or Cc.) of formaldehyde solution then added, an intensely red solution of colloidal gold will result.

If a concentrated solution of sodium silicate be treated with hydrochloric acid and the resulting sodium chloride and excess of hydrochloric acid be then removed by means of dialysis (see p. 180), a colloidal solution of silicic acid will result. Ferric hydroxide may be obtained in solution in colloidal form by dissolving freshly prepared ferric hydroxide in a solution of ferric chloride, and removing the latter salt subsequently by dialysis; this solution, however, is apt to gelatinize unless a small portion of ferric chloride be allowed to remain.

To some extent colloidal solutions of metals have been introduced in medicine, but their preparation is, as a rule, not within the reach of

the retail pharmacist. Thus, colloidal silver is officially recognized in the German Pharmacopœia as *Argentum Colloidale* or *Collargolum*, and a suspension of the same in fat is recognized as *Unguentum Collargoli*, or *Credé's Ointment*. Colloidal silver, or collargol, is said to contain 85 to 87 per cent. of metallic silver together with a small percentage of albumen, and occurs in the form of greenish- or bluish-black shining metallic particles, which yield a fairly stable colloidal solution with fifty times their weight of distilled water; such a liquid is not perfectly transparent, but will become so upon dilution with much distilled water.

Oxide of silver in combination with casein, the albumenoid substance contained in milk, has been placed on the market under the name *Cargentos*, and occurs in odorless and tasteless black scales of metallic luster, which yield with distilled water colloidal solutions, or rather suspensions, appearing reddish-brown by transmitted light and greenish-black by reflected light.

Colloidal calomel has been obtained by decomposition of a solution of sodium chloride in the presence of albumen or some other proteid, with mercurous nitrate, and precipitation of the colloidal mercury compound in combination with albumenoids, by means of alcohol. The name *Calomelol* has been given to this new colloidal product. It occurs as a grayish, tasteless powder, containing 80 per cent. of mercurous chloride and about 20 per cent. of albumenoids, which forms an opalescent solution with water, but is insoluble in alcohol and in ether.

It is well known that certain compounds of copper, gold, iron, mercury and silver will fail to be precipitated in the presence of acacia, albumen, casein, gelatin, starch, etc., and even sugar. At one time it was assumed that the presence of these normal colloids prevented chemical reaction, but it has been shown that reaction does take place and that the minute particles of the newly formed compound are prevented from aggregating by the normal colloids present in hydrated form. Thus: If a solution of mercuric chloride be added to a mixture of mucilage of acacia and lime water, no precipitation of yellow mercuric oxide will occur, although after standing for a day or longer a deposit of mercurous oxide and metallic mercury takes place, but if the original mixture be poured into 95 per cent. alcohol a yellow precipitate is formed mixed with the precipitated acacia. If weak solutions of silver nitrate and of hydrochloric acid, each containing 1 per cent. of gelatin, are mixed, silver chloride is not precipitated, but remains in colloidal suspension and will pass through a paper filter in form of an opaque liquid; neither does boiling cause separation of the new silver compound.

Solvents or Menstrua.—The liquids used as solvents or menstrua in pharmacy are water, alcohol, glycerin, ether, chloroform, and occasionally diluted acids and alkaline solutions, as well as fixed and volatile oils; each of these fluids has a specific action, and their use

gives rise to different classes of solution designated as infusions, tinctures, wines, etc. *Water* is more extensively employed than any other solvent; nearly all the salts of the alkalies, earths, and metals are dissolved by it, together with a large number of vegetable acids and the salts of the alkaloids. *Alcohol* is an excellent solvent for vegetable substances, such as resins, volatile oils, glucosides, and alkaloids; it also possesses valuable negative properties, since it does not dissolve gum, starch, and albumen, which impair the stability of aqueous solutions. The combined solvent powers of alcohol and water are utilized in the form of diluted alcohol or wine as a menstruum for numerous liquid vegetable preparations. *Glycerin* is chiefly employed to insure the permanency of vegetable solutions when the use of alcohol is contraindicated; it is also an excellent solvent for the tannins, pepsin, and some mineral salts and vegetable acids, and forms the basis of a valuable class of solutions known as *glycerites*. The use of *ether* is confined to solutions of fixed oils and fats, volatile oils, and resins, and some alkaloids and neutral principles. *Chloroform* is employed as a solvent for phosphorus, the active constituents of some drugs, as cantharides, as well as the substances mentioned above under ether, possessing the advantage over the latter of non-inflammability and a higher boiling point. *Acids*, such as acetic, hydrochloric, and sulphuric, are used in connection with water or water and alcohol to facilitate the solution of active principles in drugs like cinchona, nux vomica, ergot, sanguinaria, squill, etc., and also to preserve better the resulting solutions. *Alkalies* are employed as solvents for resinous bodies, but to a limited extent only, and the use of *fixed* and *volatile oils* is restricted to very few substances, chiefly in connection with liniments and ointments.

The process of treating a mixture of soluble and insoluble mineral substances with solvents which only partially dissolve them is termed *lixiviation* or *leeching*, and is extensively practised in the arts; as an example may be cited the leeching of ashes of wood and marine plants for the purpose of dissolving out the alkali carbonates, iodides, etc. The various methods of partial solution applied to mixtures of soluble and insoluble vegetable matter are usually comprised under the general term "extraction," but have received specific names, such as infusion, decoction, maceration, digestion, and percolation.

The process of *Infusion* is understood to represent the solvent action of boiling water on vegetable drugs during the time occupied in cooling; it may be varied, as to a longer or shorter period of time, according to the degree of extractibility of the principles to be dissolved, and should always be conducted in closed vessels. The substance to be infused should be in a coarse state of division and preferably suspended in the liquid. *Decoction* represents the solvent action of fluids at their boiling temperature, and is confined to drugs not yielding their active virtues at a lower temperature and where no loss of volatile principles need be feared. *Maceration* consists in

subjecting a mixture of soluble and insoluble matter in a divided state to the solvent action of fluids at ordinary temperature for such length of time as may be necessary to insure complete solution of the principles sought; the process must be conducted in well closed vessels, and the contents must be well shaken at least once in twenty-four hours. Frequent agitation is essential if complete extraction of soluble matter is to be insured by maceration, as otherwise a dense layer of a concentrated solution will soon envelop the material and prevent the solvent action of the menstruum from being effective; hence only a small proportion of the soluble constituents will be taken up, as may be readily observed in the slight color and odor of the supernatant liquid if a mixture of asafetida and alcohol, or of opium and water, be set aside for a week *without agitation*. *Digestion* differs from maceration only in the higher degree of temperature employed, it being constant during the process, the use of which is confined to substances of very close texture.

Sterilization of Solutions.—All solutions, such as aromatic waters, infusions, syrups, etc., are liable to contain microörganisms derived from the air. To some extent the stability of such solutions is endangered by the presence of the microörganisms, and in other cases such infected solutions may seriously affect the patient when used. It is, therefore, desirable to subject solutions intended for hypodermatic use or instillation into the eye to a process of sterilization by means of heat for the purpose of destroying the microörganisms present, and then to preserve them in sterile containers. The Pharmocopœia gives official directions for sterilization as follows:

Solutions which are not liable to suffer injury at the temperature of boiling water can be sterilized by heating them in properly stoppered bottles or flasks, previously washed with very dilute (1 per cent.) hydrochloric acid and then thoroughly rinsed with water for the purpose of removing any alkali possibly in the glass, in a current of live steam for thirty to sixty minutes, preferably on three successive days. After the operation the lip and stopper of the vessel should be covered with sterilized parchment paper, or the container may be wrapped in parchment paper before starting sterilization, which should not be removed until the solution is to be used. If a pressure apparatus or autoclave (see Figs. 100 and 101) be used, exposure for twenty minutes to a temperature of 115° to 120° C. will, as a rule, prove sufficient.

Solutions of substances which can not be exposed to the above treatment without danger of decomposition, such as solutions of certain alkaloidal salts like cocaine hydrochloride, physostigmine salicylate, etc., can be rendered approximately sterile by preparing them with sterilized distilled water in previously sterilized containers; moreover all utensils required in making the solution, such as scale pans, spatulas, glass mortars, etc., should be sterilized immediately before use, either in a current of steam or by thoroughly cleaning them with purified

cotton saturated with alcohol, followed with purified cotton saturated with ether. If filtration is necessary, this must be conducted with sterile filter paper in a sterilized funnel and under cover.

Porcelain filters, such as the Berkefeld Filter, may also be used for the purpose of rendering solutions sterile, after they have been tested and found to remove all microörganisms from a liquid filtered through them.

Among the solvents used, distilled water is easily sterilized by boiling it in a sterilized flask, closed with a pledget of absorbent cotton, for thirty minutes or an hour; glycerin may be sterilized by heating in a current of live steam for an hour, while oil is best heated for two hours in a hot-air oven at 120° C. Alcohol, ether and chloroform do not require sterilization, as they themselves destroy the life of bacteria and other microörganisms.

Glass or metal containers and other utensils may be sterilized by heating them for two hours in a hot-air oven at 160° to 170° C. Corks should never be used for stoppering containers during the process of sterilization, as only rubber stoppers are suitable for sterilization, since the latter are not affected by dry or moist heat like cork.

FIG. 100.

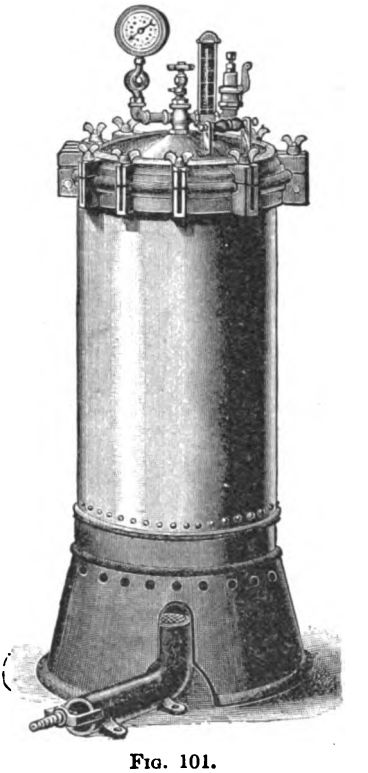


FIG. 101.

In hospitals and some large pharmacies it may be desirable to keep on hand sterilized solutions for immediate use, and in such cases the following suggestions of Kraemer will be found useful: Any bottle of convenient size, 8 oz., 16 oz., or 32 oz., may be fitted with a doubly perforated rubber stopper through which two glass tubes are to be passed, which are bent at right angles and the free ends directed downward, experience having shown that microörganisms in air tend downward rather than to rise, and thus entrance into the

tubes is obviated. The tube through which the air is forced for expelling the liquid has a bulb blown near the end, which is provided with a plug of sterilized cotton for filtering the air, and pressure is produced by means of an atomizer bulb. The bottle, having been washed and then rinsed with sterilized water, is allowed to drain, and when dry is heated in a hot-air oven for thirty to forty-five minutes at a temperature of 130° to 150° C. (266°–312° F.).

The solution, immediately after having been prepared, is poured into the sterilized bottle, and the latter closed with a plug of sterilized cotton and a cap of paper placed over the mouth. It is then placed in a steam sterilizer and heated at 100° C. (212° F.) for thirty minutes on three consecutive days.

FIG. 102.

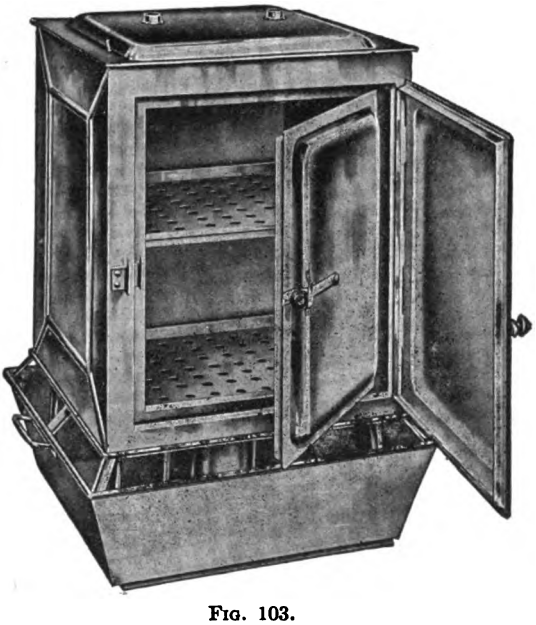


FIG. 103.

The rubber stopper and glass tubes are sterilized in a steam sterilizer for forty-five minutes at 100° C. (212° F.) and are introduced into the bottle previous to heating it and its contents for the third time, the paper cap and cotton plug having been removed.

When cool the solution can be used as needed by simply attaching the atomizer bulb and operating it in the usual way.

The steam sterilizers made by Arnold & Co., of New York (see Figs. 102 and 103), will be found very convenient for small operations, especially for sterilizing extemporaneously prepared solutions. The apparatus shown in Fig. 102 can of course be used only for steam sterilization, and the temperature is limited to 100° C., whereas the one shown in Fig. 103 may be used either for steam or dry heat, being provided in the latter case with a special extra appliance.

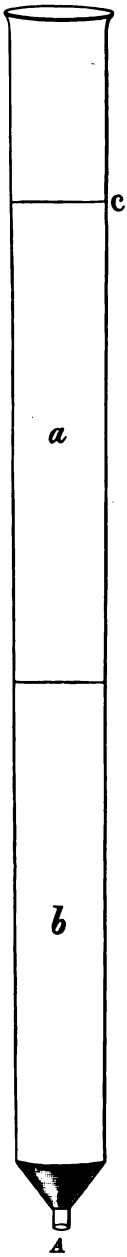
CHAPTER VIII.

PERCOLATION.

PERCOLATION, or, as it is sometimes called, displacement, is beyond doubt the most important method of solution or extraction in the hands of the pharmacist. The term percolation (from the Latin *per* and *colo*, meaning to strain or trickle through) may be defined as a process whereby the soluble constituents of vegetable drugs are extracted by allowing the menstruum to permeate a column of the more or less finely powdered material, the saturated solution being removed as fast as formed, thus continually presenting fresh solvent to the drug. The apparatus in which the process is carried on is known as the *percolator*, the solution obtained as the *percolate*, and the residue of insoluble matter as the *marc*.

Although the idea of solution by percolation did not originate in this country, its present improved and general application is due entirely to American enterprise and ingenuity. The first attempt to extract soluble matter from powdered drugs by allowing a menstruum to exert its solvent action during its passage through a column of the material was made by Count Real in the early part of the nineteenth century, the principle involved being about the same as that utilized by the French in the preparation of their world-renowned coffee. In 1833 M. Boullay, an enterprising French pharmacist, considerably modified the plan of Count Real, and in a series of carefully conducted experiments demonstrated the adaptability of the process of percolation to the extraction of vegetable drugs. So convincing were the results of his investigations that William Procter, Jr., and A. Duhamel, prominent American pharmacists, became deeply interested in the work, and in 1839 strongly advocated its adoption as a method of extraction superior to others known at that time. Although the process of percolation was recognized in the United States Pharmacopœias of 1840 and 1850, it did not meet with the general favor since accorded it until Prof. Israel Grahame, of the Maryland College of Pharmacy, in 1858, suggested some valuable improvements, which led to better results than had yet been obtained. To Prof. Grahame belongs the credit of first advocating the use of powders of uniform degree of fineness as well as the proper moistening of the powdered drug with a sufficient quantity of the menstruum before packing it in the percolator, both of which suggestions are now considered indispensable to successful percolation; at the same time, the use and advantage of a common funnel for the percolation of many drugs was pointed out. The advantage of properly moistening the

powdered drug before packing will be readily understood when it is considered that the material to be operated upon is not a mere mechanical mixture of soluble and insoluble matter, but that the soluble principles to be extracted are intimately held or enclosed by the insoluble cellular tissue, and that penetration of the tissue by the menstruum is necessary to effect solution; the saturation of the powder with the liquid prepares the constituents for ready solution and establishes an affinity between the cellular contents and the fresh menstruum, enabling the latter to permeate the cells by osmotic action. If the menstruum is brought in contact with dry powder, absorption of the former either takes place very slowly or is entirely interfered with, just as dry, hard sponge resists the entrance of water for a long time; the original moist condition of the drug before it was powdered must therefore be re-established before the menstruum can exercise its power of extraction.



The principle underlying the process of percolation may be stated as follows: A solvent or menstruum, poured on the top of a mass of powder consisting in part of soluble matter, supported on a porous diaphragm in a cylindrical or conical vessel, descends from layer to layer by reason of its own gravity and the pressure of the superincumbent liquid, penetrating the particles of powder by reason of surface action, and exercising its solvent power on each successive layer until its power of solution is exhausted, after which it continues its downward flow, as a saturated solution, into the receiving vessel below. This process continues until all soluble constituents have been removed from the powder, the descending menstruum becoming less and less charged with extractive matter. To insure such complete extraction it is absolutely necessary that the material operated upon shall be in a uniform powder and that the capillarity or porosity of the mass be not interfered with in any way, so that the descent of the menstruum may be slow, even, and regular from one horizontal layer to the next.

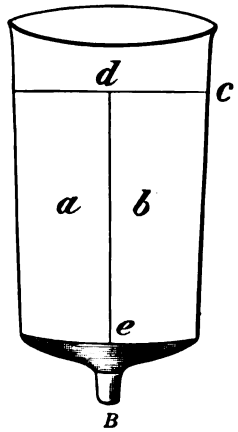


FIG. 104.

Different styles of percolators have been proposed at various times, and as drugs vary in their nature and require different treatment to

yield different preparations, the pharmacist must be supplied with a variety of percolators, from the conical shape of the ordinary funnel to the nearly cylindrical. The choice of percolator depends largely upon the character of the percolate to be obtained, and also upon the nature of the drug; for instance, if a very strong solution is to be prepared with a minimum quantity of menstruum, a narrow cylindrical percolator is preferable, so that the solvent is made to pass through a long column of the drug and thus become thoroughly saturated; a cylindrical, or only slightly tapering, percolator is also indicated when the menstruum is strongly alcoholic, or when ether or some other volatile liquid is used for extraction. The advantage of using a long, narrow percolator with the view of economizing menstruum when concentrated vegetable solutions are to be made, may be easily demonstrated by means of two percolators having the same cubical capacity, but of such difference in shape that the diameter of the one shall be exactly one-half the diameter of the other, and that the narrower percolator shall be four times as long as the other, as shown in Fig. 104, *A* and *B*. Suppose a given quantity of drug is packed into *A* and fills the same up to the line *c*, and then a like quantity of drug be packed into *B;* if we assume the mass in *A* to be divided into two equal sections, *a* and *b*, by means of the plane *de*, it is fair to assume that the same quantity of material in the respective sections *a* and *b* when packed in *B*, instead of occupying adjoining spaces as in *A*, would lie one above the other. If it requires 10 liters of menstruum to exhaust completely the drug in *A*, it may be assumed that the sections *a* and *b* required equal amounts, or 5 liters each. If 5 liters of menstruum be now poured upon the column of drug in *B*, this quantity of menstruum will prove sufficient to exhaust completely the upper section *a*, as the same quantity of solvent proved adequate for the complete exhaustion of an identical quantity of drug in *A;* but the solvent powers of the menstruum will not have been entirely spent, and hence as it passes downward through the lower section *b* it will continue to extract soluble matter until fully saturated, and then flow off into the receiving vessel. All the soluble matter in *a* and a portion of that in *b* having been taken up by the 5 liters of menstruum used, another portion of menstruum is poured on the top of the column, and as there is no soluble matter left in *a*, it will be necessary only to extract the soluble matter still remaining in *b*, for which purpose 2 or 3 liters of menstruum will suffice. Thus in connection with percolator *B*, 7 or 8 liters of menstruum are found sufficient to exhaust completely a quantity of drug which in percolator *A* was found to require 10 liters of menstruum, showing a saving of about 20 or 30 per cent. If, on the other hand, the quantity of drug to be extracted is small in proportion to the menstruum, as in the majority of official tinctures, a wider percolator, of the shape and style shown in Fig. 105, may be used, in which the liquid will traverse the column of drug more rapidly and yet be able to exhaust it thoroughly, owing to the larger amount

of menstruum at the disposal of the operator. When drugs such as gentian, senega, rhubarb, orange peel, and others, which have a tendency to swell considerably, particularly with aqueous or feebly alcoholic menstrua, are to be percolated, a common funnel will often be found advantageous on account of the ample allowance for lateral expansion of the moist drug. The size of the percolator selected should be in proportion to the quantity of drug to be extracted; when properly packed in the percolator the drug should not occupy more than about three-fourths of its height.

FIG. 105.—Ordinary glass percolator.

FIG. 106.—Covered tin percolator, with stopcock for regulating the flow.

The covered tin percolator (Fig. 106) consists of a cylinder varying in size and tapering somewhat toward the funnel-shaped end, provided with two perforated diaphragms fitting loosely into the cylinder, the lower of which should be more finely perforated than the upper. The stopcock in the neck of the funnel serves the double purpose of allowing maceration for any desired period and of enabling the operator to regulate the rate of flow of the percolate. Tin percolators cannot be used, however, for any drugs containing principles liable to be affected by metal, or to be exhausted with acid menstrua.

Fig. 107 represents the Oldberg percolator, introduced in 1884, and especially designed for use in the preparation of fluidextracts. These percolators are now made of heavy glass in nine sizes, varying

from 240 to 7000 milliliters (or cubic centimeters), about 8 fluid-ounces to 2 gallons, capacity. They are used extensively, and are admirably adapted for the exhaustion of drugs with a minimum quantity of menstruum.

For percolation with very volatile liquids—ether, chloroform, and the like—a specially constructed percolator must be used (see Fig. 108), in which proper provision is made to prevent loss of menstruum and to establish communication between the vessel intended to receive the percolate and the space above the drug in the percolator, so that the air may pass upward when displaced by the percolate in the receiving jar; this latter provision is essential to successful percolation. As may be seen from the illustration, the percolator is

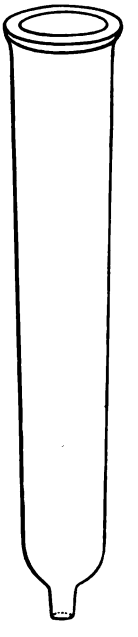


FIG. 107.—Oldberg percolator.

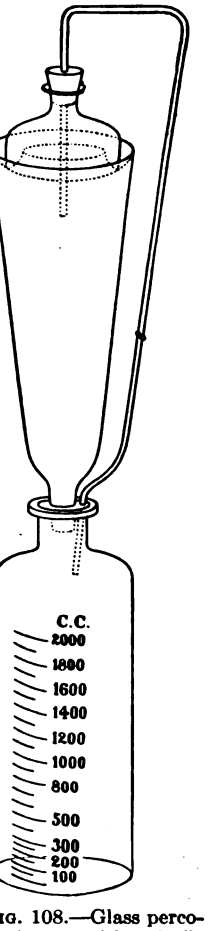


FIG. 108.—Glass percolator for use with volatile menstruum.

fitted air-tight to the receiving vessel by being passed through a cork, and loss of menstruum at the top is prevented by a water joint with which the cover of the percolator forms an air-tight connection. The air is carried up outside of the percolator, and made to enter at the top, to take the place of menstruum passing downward through the drug. Fresh menstruum may be supplied through the opening in the cover

without disturbing the water joint. Another plan for percolating with chloroform, ether, and similar volatile menstrua is to pass a tube through the center of the percolator and extending below the lower diaphragm, which provides for the upward displacement of the air from the receiving vessel, the drug being packed around the tube; in such cases the percolator must be provided with an air-tight cover, and the exit tube must also pass air-tight through a cork in the neck of the receiving jar. An arrangement of tubing on the outside, as seen in Fig. 108, may be attached to any percolator capable of being closed air-tight at the top with a cork.

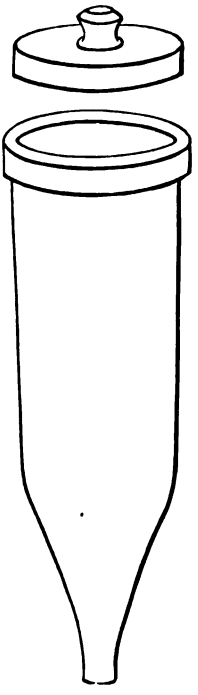


FIG. 109.—The Dursse percolator.

In 1874 the Dursse percolator was introduced (see Fig. 109). It combined the advantages of a broad cylindrical and a conical vessel, and was admirably adapted for quantities of drug ranging from 400 to 600 Gms. Unfortunately but one size was made of this pattern, which is 15 inches in length, 5 inches in diameter at the top, and 1 inch at the beginning of the outlet tube. One of these percolators was in use almost weekly, during eighteen years, in the author's hands, and many pounds of nux vomica, cinchona, ergot, ginger, vanilla, gentian, rhubarb, valerian, etc., were successfully extracted therein during that time. Its chief merits lie in the perfect uniformity of its sides and its accurately fitting cover, by which the flow of the liquid can be regulated and all volatilization of menstruum be prevented. Being made of heavy glass, it bears usage very well and is not easily broken.

Manufacturers who operate upon large quantities of drugs varying from 25 to 500 pounds or more, employ percolators made of heavy tinned iron or copper, either tin- or porcelain-lined. Such percolators are usually of the shape and style shown in Figs. 110 and 111, and are intended to be supported either in heavy frames or on heavy blocks at such height from the floor as to permit of the convenient use of receiving bottles. These larger percolators are provided with two diaphragms or perforated disks, likewise made of heavy tin; the one is placed about 8 or 10 inches from the bottom, and is usually covered with a piece of muslin before the moistened drug is introduced, while the other diaphragm is inserted over the mass of drug, which has been previously covered with a piece of felt or flannel to insure uniform distribution of the menstruum. In order that the descent of the menstruum may be regular and uninterrupted during maceration of the drug, a tube attached to the inner side of the percolator connects the

space below the lower diaphragm with the space above the upper disk, and thus allows the air from below to displace the menstruum above. As shown in the illustrations, these percolators are frequently provided with an inclined bottom intended to permit the ready passage of the percolate to the faucets, which latter also serve to regulate the flow of the liquid, and thus collection of the percolate on the bottom of the percolator is avoided. A well fitting cover prevents evaporation of alcohol and admits fresh menstruum when desired. Fig. 112 shows a series of large percolators suspended from the ceiling by

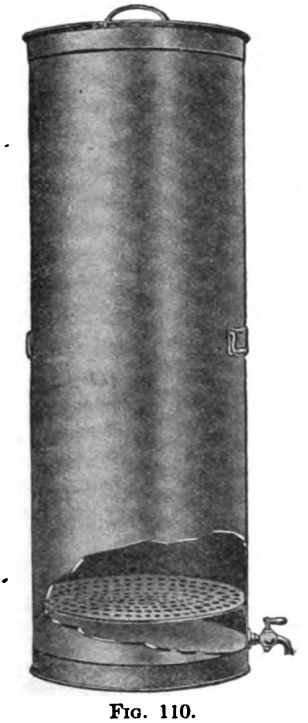


FIG. 110.

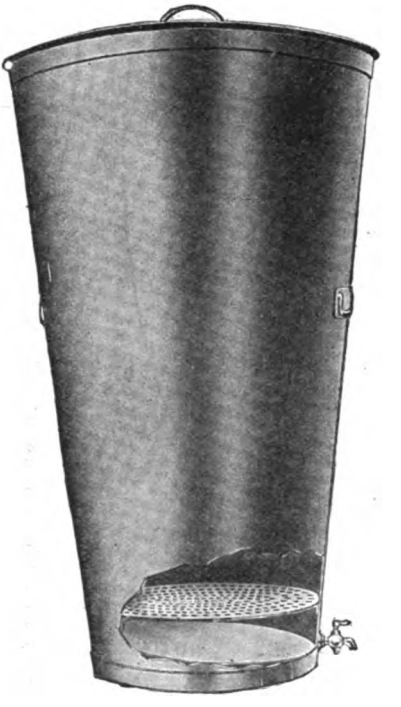


FIG. 111.

Large percolators, made by the Arthur Colton Co., Detroit, Mich.

trunnions, as used in some of our large manufacturing establishments; this method is very convenient for handling the apparatus, and facilitates the emptying of the marc at the end of the operation direct into large vessels for transfer into dreg stills.

The well known siphon or well-tube percolator, suggested in 1872 by the late Dr. E. R. Squibb, is extensively used in the laboratories of some manufacturers; the principle involved, with slight modifications, has been adopted in the official direction for percolation in the United States Pharmacopœia since 1880. The Squibb well-tube percolator, as shown in Fig. 113, is constructed upon the principle of an artesian

well, the moistened drug representing the soil, through which the menstruum passes very slowly, the solution or percolate, rising in the well tube which passes through the center of the mass, being

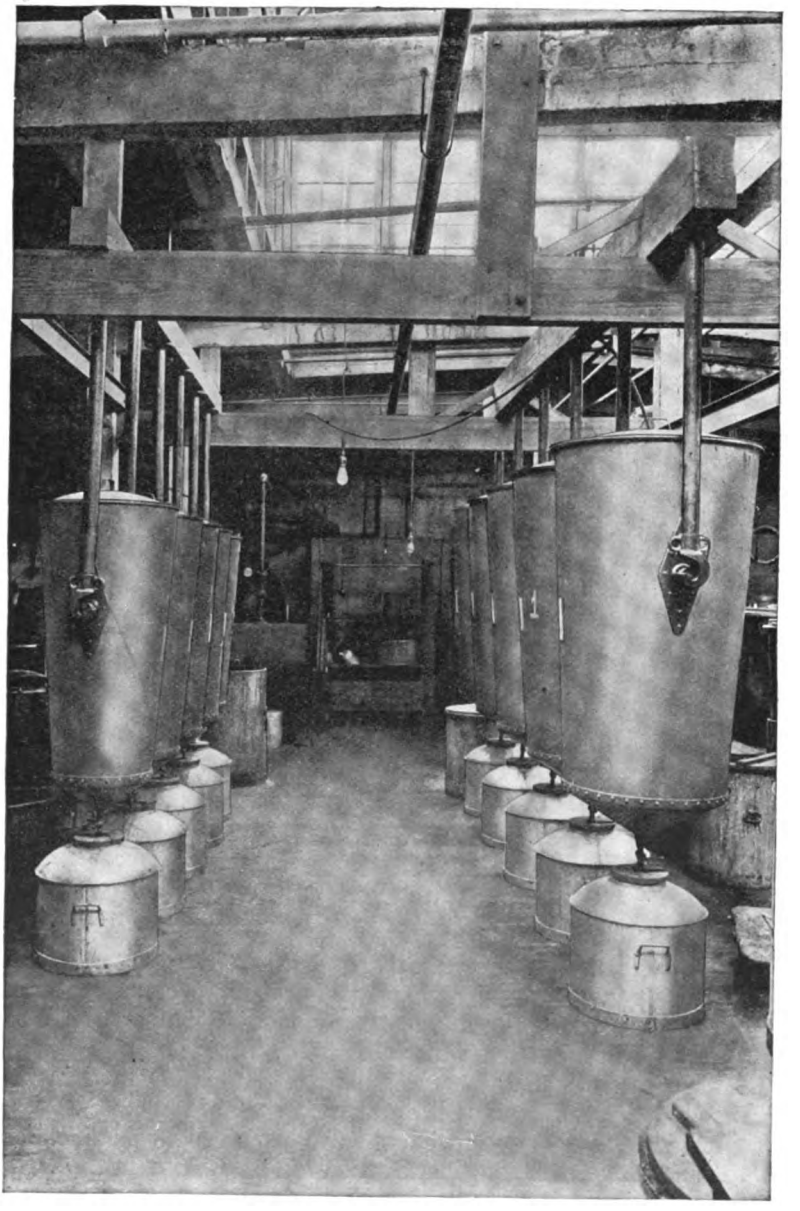


FIG. 112.—Percolators as arranged in large manufacturing establishments.

finally drawn off by the means of the glass siphon. The process is completely under the control of the operator as regards the rate of flow of the percolate and maceration of the mass to any desired extent. To prevent particles of drug from entering the well tube, this is made to rest on several disks of flannel, through which the percolate must pass before it can enter the tube. The siphon acts automatically after it has once been started, and cannot exhaust itself, because when the liquid in the percolator falls to the level of the turned-up end of the outer limb of the siphon the flow ceases, leaving the siphon-tube full of liquid, the difference in the length of the two limbs of the siphon being only such that the inner limb reaches the bottom of the well tube,

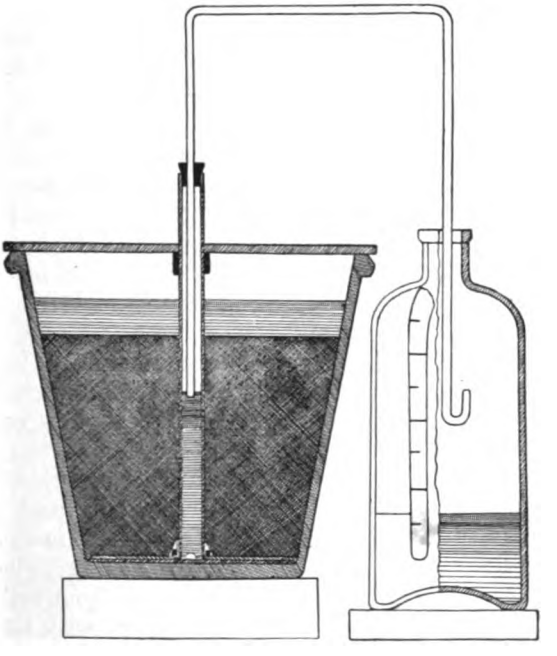


FIG. 113.—Squibb's well tube percolator, made of stoneware.

and when measured on the outer limb, reaches to one-half of its turned-up end. The pressure on the surface of the moistened drug being duly counterbalanced by the atmospheric pressure on the column of percolate in the well tube and siphon, all particles of the mass in the percolator will be subject to uniform pressure; thus the gravitation of the liquid is used to best advantage, just as in the case of the rubber tube recommended in the pharmacopœial directions for percolation. The body of the percolator may be made of glass or stoneware, and the evaporation of menstruum prevented by a tightly fitting cover of sheet rubber about ¼ or ½ inch thick.

Much has been written about "pressure percolators," the chief

claim advanced for their use being the complete extraction of drugs with less menstruum than by ordinary methods, which applies to the preparation of concentrated solutions, such as fluidextracts. The idea of more complete solution by means of pressure originated with Count Real about 1815, and the apparatus devised by him (see Fig. 114) bears a close resemblance to some of the pressure percolators of later days, devised by Rosenwasser, Berry, Suit, and Anderson. In the more recent apparatus the drug to be extracted is confined, by means of a suitable screw arrangement, between perforated disks, in any desired space, without the possibility of expansion on coming in contact with the bulk of the menstruum. The solvent is forced through the mass by pressure obtained from a column of liquid 10 or 12 feet in height, supplied by a reservoir.

FIG. 114.—The "Count Real" pressure percolator.

Management of the Process of Percolation.—The Pharmacopœia gives the following directions for conducting percolation, which are applicable to all official preparations in which this method of solution is indicated, as in each individual case the fineness of powder, and the degree of firmness with which it is to be packed are specified:

"The percolator most suitable for the quantities contemplated by the Pharmacopœia should be nearly cylindrical or slightly conical with a funnel-shaped termination at the smaller end. The neck of the funnel end should be rather short, and should gradually and regularly become narrower toward the orifice, so that a perforated cork, bearing a short glass tube, may be tightly wedged into it from within until the end of the cork is flush with its outer edge. The glass tube, which must not protrude above the inner surface of the cork, should extend from 3 to 4 cm. beyond the outer surface of the cork, and should be provided with a closely fitting rubber tube, at least one-fourth longer than the percolator itself, and ending in another short glass tube, whereby the rubber tube may be so suspended that its orifice shall be above the surface of the menstruum in the percolator, a rubber band holding it in position.

"The percolator is prepared for percolation by gently pressing a small tuft of cotton into the space of the neck above the cork, and this may then be moistened by pouring a few drops of the menstruum upon the cotton, to facilitate the passage of the first portion of the percolate, which is often very dense.

"The powdered substance to be percolated (which must be uniformly of the fineness directed in the formula, and should be perfectly air dry before it is weighed) is put into a suitable dish, sufficient menstruum is poured on, and it is thoroughly stirred with a spatula or other suitable instrument until it appears uniformly moistened. The moist powder is then passed through a coarse sieve—No. 40 powders and those which are finer requiring a No. 20 sieve, while No. 30 powders require a No. 15 sieve for this purpose. Powders of a less degree of fineness usually do not require this additional treatment after the moistening. The moist powder is now transferred to a sheet of thick paper and the whole quantity poured from it into the percolator. It is then shaken down lightly and allowed to remain in that condition for a period varying from fifteen minutes to several hours, unless otherwise directed; after which the powder is pressed by the aid of a plunger of suitable dimensions, more or less firmly in proportion to the character of the powdered substance and the alcoholic strength of the menstruum; strongly alcoholic menstrua, as a rule, permitting firmer packing of the powder than those weaker. The percolator is now placed in position for percolation, and the rubber tube, having been fastened at a suitable height, the surface of the powder is covered by an accurately fitting disk of filter paper, held in place by a glass stopper or percolator weight, and a sufficient quantity of the menstruum poured on through a funnel reaching nearly to the surface of the paper. If these conditions are accurately observed, the menstruum will penetrate the powder equally until it passes into the rubber tube, and reaches in this a height corresponding to its level in the percolator which is now closely covered to prevent evaporation. The apparatus is then allowed to stand at rest for the time specified in the formula.

"To begin percolation, the rubber tube is lowered and its glass end introduced into the neck of a bottle previously marked for the quantity of liquid to be received, if the percolate is to be measured, or of a tared bottle if the percolate is to be weighed; and by raising or lowering this receiver the rapidity of percolation may be increased or lessened, as may be desired. A layer of menstruum must constantly be maintained above the powder, so as to prevent the access of air to its interstices, until all has been added or the requisite quantity of percolate has been obtained. This is conveniently accomplished, if the space above the powder will admit of it by inverting a bottle containing the entire quantity of menstruum over the percolator in such a manner that its mouth may dip beneath the surface of the liquid, the bottle being of such a shape that its shoulder will serve as a cover for the percolator. (For illustration of the official process, see Fig. 115.)

"It is obvious that the success of the process of percolation largely depends upon the regulation of the flow of the percolate; if this should be too rapid, incomplete exhaustion will result; but if too

slow, valuable time may be wasted. The rate of flow for extracts and fluidextracts for 1000 Gms. of powder should range from 2 to 5 drops a minute; for official quantities of tinctures and preparations of about the same strength from 8 to 15 drops a minute; it is evident

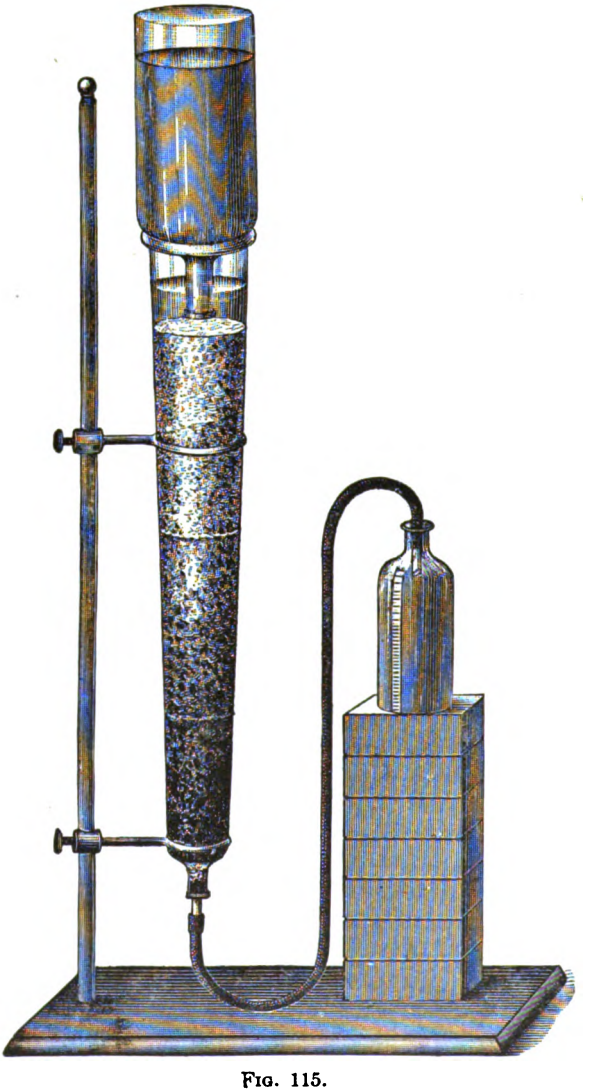


FIG. 115.

that the proper rate of flow should vary with the quantity and character of the drug employed and the density of the menstruum."

The degree of fineness of powder to which a drug is to be reduced depends partly upon the menstruum to be used and partly upon the

nature of the active constituents of the drug and the readiness with which these can be extracted. Drugs like aconite, cinchona, nux vomica, veratrum viride, and others, require to be in fine powder; while gentian, rhubarb, krameria, squill, and the like, can be readily exhausted in coarser powder. As a rule, strongly alcoholic or ethereal menstrua are used with fine powders, whereas hydroalcoholic and aqueous menstrua are better adapted to coarser powders.

The quantity of menstruum to be used for moistening the powder also varies with different drugs; one-fourth to one-half as much menstruum as powder is generally required to dampen it thoroughly without destroying its mobility, depending likewise upon the nature of the drug and menstruum. In a few cases, where the active constituents are quickly extracted, and previous moistening might cause the powder to agglutinate, as in the case of the official oleoresins, it is even better not to moisten the drug at all before placing it in the percolator.

The next step is the proper packing of the percolator, and upon it will largely depend the success of the process. A suitable support must be provided for the moistened powder, and for this purpose a notched cork or a tuft of absorbent cotton may be used. If cork be chosen, a layer of cotton should be placed over it to prevent the escape of powder; or if cotton alone be used, it may be slightly compressed into the neck of the percolator. Unless the quantity of drug be large, the moistened powder, after having been first passed through a coarse sieve to break up any lumps, should be transferred to the percolator *all at one time*, and then shaken down by tapping the sides of the vessel. If the drug is to be saturated with menstruum before maceration, as in the case of fluidextracts, the powder should be at once compressed, moderately or firmly, as the character of the menstruum and the nature of the drug may require. As a rule, fine powders and alcoholic menstrua demand firm packing, as also ligneous and spongy drugs under certain conditions; aqueous menstrua generally necessitate moderate compression. If the moistened drug be introduced in layers, uniform packing becomes more difficult; the lower portions of the drug should be less firmly compressed than the upper layers, because the menstruum, when it reaches them, being already charged with some soluble matter, is denser than at the top, and hence cannot penetrate a firmly packed mass as readily as would fresh menstruum. Maceration of the moistened powder prior to percolation is advantageous in the majority of cases, as it allows the drug to swell and become more thoroughly permeated by the menstruum, and permits more satisfactory packing afterward; in some cases, where concentrated solutions are desired, maceration after saturation is positively necessary to insure good results. The packing of the moistened powder is best effected with a packing stick of suitable design, made of hard wood, of the shape of the well known potato masher. Next to uniformity in fineness of powder, uniformity in packing is the most important feature in percolation, so as to insure the even descent of the men-

struum; if the drug is more firmly compressed on one side than on the other, the menstruum is sure to flow in the direction of least resistance, and leave a part of the mass imperfectly extracted. After the powder has been packed, a diaphragm of filter paper or felt is laid over the surface and kept in place by means of pebbles, glass marbles, or pieces of broken glass; this is for the purpose of preventing disturbance of the upper layer and to insure equal distribution of the liquid when the menstruum is poured on.

As stated in the pharmacopœial directions, a layer of menstruum must constantly be maintained above the powder, in order to prevent access of air to its interstices. Every percolator should be provided with a cover, which may be either of glass or sheet rubber, to avoid loss of or change in the menstruum.

The simplest arrangement for controlling the rate of flow of the percolate is by means of a rubber tube, as specified in the official directions, and this device can be attached to nearly every form of percolator known. As the rate of flow from the tube will be proportionate to the difference in height between the liquid in the percolator and the point to which the tube is raised on the outside, it is evident that its control is within easy reach, and may be varied from a constant stream to 2 drops per minute. The rapidity with which the percolate shall be allowed to pass will vary with the object in view and the ease with which the active principles enter into solution; for tinctures, the average rate may be stated to be 8 to 15 drops per minute, while the percolate in the case of fluidextracts should not be allowed to flow faster than from 2 to 5 drops per minute.

The complete exhaustion of a drug can only be determined by examination of the last portions of the percolate; hence a thorough knowledge of the valuable constituents sought to be extracted is essential, since absence of color and odor is not always indicative of perfect exhaustion. In the case of aromatic drugs like cardamom seed, cloves, ginger, vanilla, and others, the absence of odor and taste other than those of alcohol, in the last portion of the percolate, is an indication of the complete extraction of the constituents desired. Drugs like cascara sagrada, gentian and quassia, possessing a decided bitter taste, and drugs like catechu, geranium and krameria, which owe their medicinal value to the presence of astringent principles, are known to be entirely deprived of their active constituents when the last portion of the respective percolates is found free from the characteristic taste of the particular drug in question. Resinous drugs, such as cimicifuga, jalap and podophyllum are known to have yielded all of their resinous constituents to the menstruum employed, when a few drops of the last portion of the percolate allowed to fall into cold water fail to cause any opalescence or turbidity.

Alkaloidal drugs, such as aconite, belladonna, cinchona, pilocarpus, etc., are preferably tested by chemical means for complete, or at least practically complete, extraction of their active principles, as

follows: A small quantity of the percolate is collected separately near the end of the operation, acidulated with sulphuric acid and warmed in a beaker or glass dish on a waterbath until all alcohol has been dissipated. If a drop or two of the official potassium mercuric iodide solution, better known as Mayer's Solution, be added to the cooled acid liquid, no precipitate or turbidity should result; the appearance of a faint cloud would indicate practical exhaustion. For better observation of the test, the beaker should be placed on a dark surface after addition of the test solution.

A considerable quantity of alcoholic menstruum is sometimes retained by the marc after exhaustion of the drug, and this may be recovered by expression or by percolation with water, either direct or after admixture with clean sawdust. Such recovered alcohol is unfit for further use until it has been purified by adding 3 grains of potassium permanganate to every pint, shaking the mixture occasionally during several days, and then decanting and distilling. Another plan to avoid the loss of alcohol by absorption is to employ gradually weaker menstrua, after the required quantity of original menstruum has all been added.

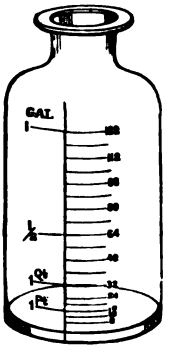


FIG. 116.—Glass receiving jar, graduated in U. S. fluid measure.

Much time and annoyance may be saved by collecting the percolate in properly graduated glass jars (if the percolate is to be weighed, use tared vessels), which can be obtained from glass manufacturers in different sizes adjusted both for apothecaries' and metric fluid measure (see Figs. 116 and 117). A convenient plan also is to paste a strip of paper on a wide-mouth bottle and mark on the same with ink the different quantities of liquid measured into the bottle, as shown in Fig. 118; to protect the paper scale and render it impervious to moisture, it should be coated with colorless varnish.

The usual method of supporting percolators is by means of the iron rings of a retort stand, as shown in Fig. 115; in order to protect the glass, sections of rubber tubing may be attached to the rings, forming suitable cushions or guards. A very convenient arrangement is Beck's percolating stand (see Fig. 119), which admits of simultaneous multiple operations and is equally well adapted for use in the store or laboratory. The stand can either be placed on the floor or be supported on two iron brackets fastened to the wall; as shown in the illustration, it can be changed by means of thumb-screws to suit various heights of bottles. The length of the base board is 42 inches, the width 12 inches, and the extreme height of the stand 36 inches; the supports for percolators and funnels are formed by means of cross pieces suitably hollowed out and secured by screws passing through the slot in the cross bars.

Repercolation.—Repercolation is a process intended for the preparation of concentrated vegetable solutions with a minimum quantity of

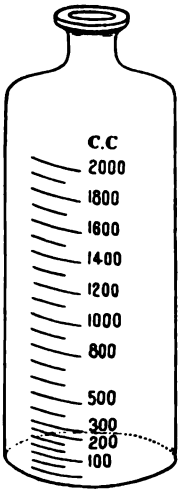


FIG. 117.—Glass receiving jar, graduated in metric fluid measure.

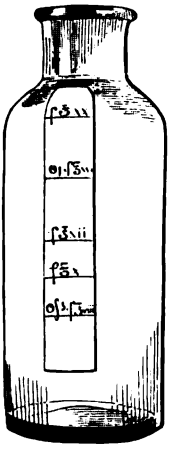


FIG. 118.—Graduated glass receiving jar, home made.

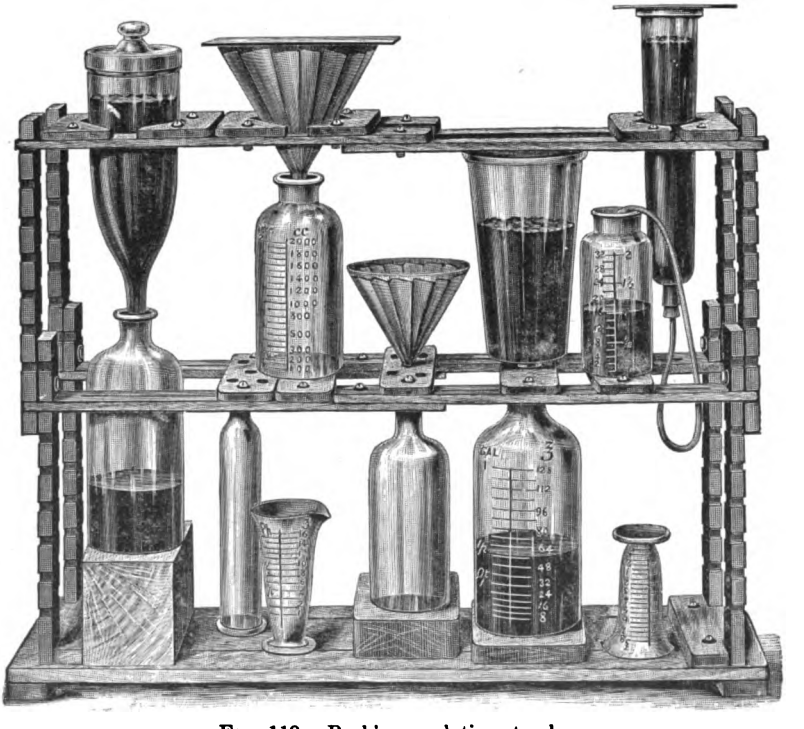


FIG. 119.—Beck's percolating stand.

menstruum, and is confined to the manufacture of fluidextracts without heat. Dr. Squibb, who was the author of the process, defined it to be "the successive application of the same percolating menstruum to fresh portions of the substance to be percolated." His suggestion was based upon the observation that a weak solution of the constituents of a drug is a better solvent for the soluble active principles of that drug than fresh menstruum. The following example will serve to illustrate the process of repercolation: 1000 Gms. of a properly powdered drug are divided into five portions of 200 Gms. each; one portion is moistened, packed, macerated, and percolated to exhaustion, the first 150 mils. (or Cc.) of the percolate being set aside as finished product, the remainder being collected in fractions of 200 mils. (or Cc.), and numbered respectively 1, 2, 3, etc., in the order in which they are collected. The second portion of the drug is moistened with No. 1 weak percolate, packed and percolated to exhaustion, the different weak percolates being used in the order in which they have been collected, followed by fresh menstruum if necessary, the first 200 mils. (or Cc.) of the percolate from this second portion of the drug being set aside as finished product, the remainder being again collected in fractions of 200 mils. (or Cc.), and numbered 1, 2, 3, etc., as before. The third, fourth, and fifth portions of the drug are treated exactly like the second portion, the first 200 mils. (or Cc.) of the percolate in each instance being set aside as finished product. When the fifth portion of the drug has been exhausted there will be on hand five lots of finished product—150, 200, 200, 200, and 200 mils. (or Cc.); total, 950 mils. (or Cc.)—and besides, four or five lots of weak percolate supposed to hold in solution the soluble matter from 50 Gms.; these weak percolates, properly numbered, are set aside, to be again used in place of fresh menstruum for the next lot of the same preparation, the process henceforth being continued exactly as directed above for the second portion of the drug. This retention of 25 per cent. of the soluble matter of one portion of the drug in the weak percolates is based on numerous carefully conducted experiments, the results of which showed that when 1000 Gms. of drug are exhausted by percolation, from 70 to 80 per cent. of the total soluble constituents present are contained in the first 750 mils. (or Cc.) of percolate.

The Pharmacopœia gives the following directions for repercolation, also known as fractional or divided percolation, which are practically identical with those first suggested by Prof. C. Lewis Diehl, in the National Formulary, for the preparation of fluidextracts.

Divide 1000 Gms. of the ground drug into 3 parts of 500 Gms., 300 Gms. and 200 Gms. respectively. The first portion (500 Gms.) is moistened with sufficient of the prescribed mestruum to dampen the drug uniformly and so maintain it after six hours maceration in a tightly covered vessel. It is then packed in a cylindrical percolator, sufficient menstruum being poured on to saturate the powder and leave a stratum of liquid above it. When the liquid begins to drop from the percolator,

the lower orifice is closed, the percolator closely covered, and the drug allowed to macerate for forty-eight hours. Percolation is then allowed to go on at a rate not to exceed 10 drops per minute, menstruum being gradually poured on to maintain a constant layer above the drug. The first 200 mils. of percolate are set aside as a reserve and percolation continued until 1500 mils. of additional percolate have been collected in successive portions of 300 mils. each. (To avoid confusion the weaker percolates should be numbered 1, 2, 3, 4, and 5.)

The second portion of the drug (300 Gms.) is moistened with sufficient of the first weaker percolate to render it uniformly damp and so maintain it after six hours maceration in a tightly covered vessel. It is then packed in a cylindrical percolator, macerated, and percolated as in the case of the first portion of the drug, but using as menstruum the weaker percolates in the order in which they were collected, followed, if these be insufficient, by some of the original menstruum. The first 300 mils. of percolate are set aside as reserve and percolation continued until 600 mils. of weaker percolate have been collected in successive portions of 200 mils. each.

The third portion of the drug (200 Gms.) is moistened with sufficient of the first portion of weaker percolate collected from the second portion of the drug to render it uniformly damp and so maintain it after six hours maceration in a tightly covered vessel. It is then packed in a cylindrical percolator, and macerated and percolated as in the case of the second portion of the drug, using as menstruum the remaining portions of weaker percolate from the preceding operation in the order in which they were collected, followed, if necessary, by some of the original menstruum. Collect 500 mils. of percolate and mix this with the two portions of reserve previously set aside, so as to bring the volume up to 1000 mils.

Continuous Percolation.—Continuous percolation is a name sometimes applied to a process of extraction which involves the exhaustion of a drug with a limited quantity of menstruum, by repeatedly vaporizing and condensing the fluid in a specially constructed apparatus, so arranged that the extracted soluble matter remains in the receiving flask, while the solvent, in the form of vapor, passes upward to a reflux condenser, and thence flows back into the percolator. This process is chiefly employed in the examination of vegetable drugs, with a view to determine their valuable constituents, and is particularly adapted to the manufacture of the official oleoresins. For description of the apparatus employed, see the chapter on Oleoresins.

CHAPTER IX.

SEPARATION OF NON-VOLATILE MATTER.

THE process of separation may be applied to non-volatile or fixed as well as volatile matter; in the former case it is understood to refer to the removal of insoluble substances, sediments, etc., from fluids holding them in suspension, and also of immiscible fluids from each other. The various operations employed for the separation of solids from fluids are termed filtration, decantation, expression, clarification, and decoloration.

FILTRATION.

By some pharmacists filtration is considered so trivial an operation as not to merit extended consideration; but, like other simple processes, it is well deserving of study, as there is room for the exercise of intelligence and ingenuity in its many useful modifications. Filtration is usually employed when the solid matter to be removed is not present in excessive quantity, and consists in submitting the mixture to the separating action of certain media which allow the fluids to pass through but are impervious to the solid particles. Sometimes filtration is also called colation or straining; but it is understood that the process of straining differs from filtration either in the less complete removal of suspended sedimentary matter from a fluid, or in the fact that the solid particles are not in fine powder and can be easily retained by coarser media than those generally employed for filtration. Colation is a favorite mode of separation when the fluid is of a viscid character. The various filtering media employed are cotton and woollen cloth, paper made therefrom, also absorbent cotton, glass, wool, asbestos, sand, and charcoal; the clear liquid passing through these media is termed the filtrate.

For straining syrups, oils, and similar fluids, filter-bags of flannel or felt are admirably adapted, as they permit a rapid passage of the liquid and effectually retain all solid matter; such filter bags are of conical shape (see Figs. 120 and 121), and are readily made, of plain or Canton flannel, by folding over a square piece in the manner indicated in Fig. 122, the line *cd* being laid over the line *ca* and united by a seam; the bag thus formed is pointed at *c* and open from *a* to *b*, the line *ac* being lapped over to form the seam. The long end projecting toward the point *b* beyond the dotted line *ef* should be removed, and four loops of heavy cord or tape attached after the edge has been

turned over; the loops will serve to suspend the filter-bag properly in a square or round frame, as shown in Fig. 123. For some purposes, as the straining of dense saline solutions or the washing and draining

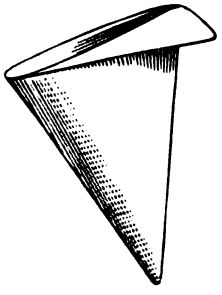


FIG. 120.—Flannel strainer.

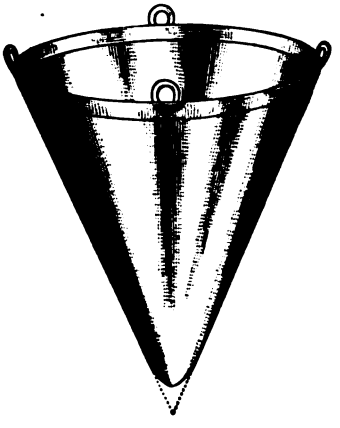


FIG. 121.—Filter-bag.

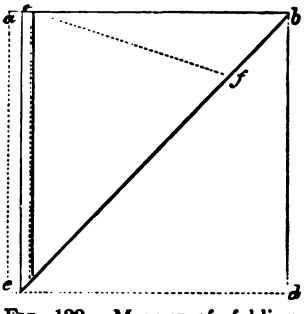


FIG. 122.—Manner of folding strainer.

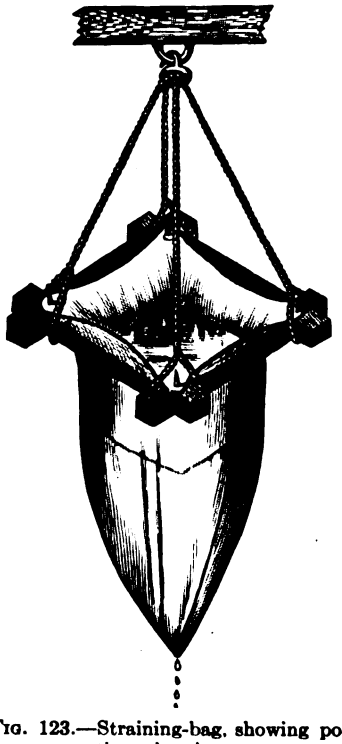


FIG. 123.—Straining-bag, showing position when in use.

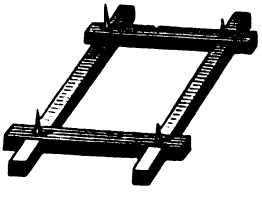


FIG. 124.—Frame for cloth or flannel strainers, known as "tenaculum."

of bulky precipitates, a square cotton cloth may be stretched over a square frame called a *tenaculum*, as shown in Fig. 124; for smaller operations, such as straining infusions or decoctions, the cloth strainer may be fastened over a funnel by means of wooden pinchcocks, and when it becomes necessary to strain with expression the ends of the strainer must be folded over and twisted in opposite directions, as shown in Fig. 125. A kind of cotton cloth known as cheesecloth is preferred by many for strainers, as it allows liquids to pass rapidly through it. All strainers should be well wetted just before they are used, and those containing sizing should be freed from the same by washing with hot water before they are put into use. For use at the dispensing counter in straining solutions, a pledget of absorbent cotton placed in the throat of a funnel will be found very convenient and serviceable; and as nearly every solution prepared is likely to contain some specks and motes, this little operation should never be neglected.

FIG. 125.—Showing the manner of folding and expressing flannel or cloth strainers.

Complete separation of fine suspended matter from fluids can best be effected by means of filtration through paper; only unsized paper should be used, the best kind being that made from cotton and linen rags, although paper made from woollen material is tougher, and, being more porous, permits more rapid filtration. The square sheets of filtering paper, which at one time were the only style to be had, are rarely used now, since cut round filters can be had of all sizes and qualities. Two kinds of paper filters are used, the *plain* and the *plaited*, the construction of which is very simple, and, when once properly understood, never forgotten. The chief advantages of plain filters are the simplicity of construction and the fact that they are admirably adapted for collecting the solid matter suspended in the fluid, which is afterward to be removed from the paper for further use; on the other hand, filtration proceeds far less rapidly in a plain than in a plaited filter, because the paper lies flat against the sides of the funnel, and the liquid passes through only at the point of apex. Plain filters are made by doubling a circular piece of filter paper upon itself, and then folding this directly in the middle; by now opening the

folds in such a manner that one sector or division shall appear on one side and three sectors on the other side, a perfect cone will be obtained, as shown in Fig. 126, which will exactly fit into a properly shaped funnel.

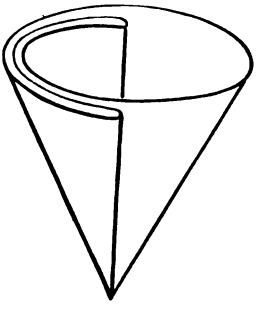


FIG. 126.—A plain filter.

The waste of paper which is caused by this method of folding a plain filter, where three thicknesses of paper are found on one side of the filter and but one thickness on the other side, may be avoided by following the suggestions of Edo Classen, which are as follows: To make a plain filter, of single thickness, which will fit a funnel having an angle of 60 degrees, use a piece of filter paper in the shape of a semi-ellipse, as shown in Fig. 127, the line AB being one-fifth longer than the line AC or AD. Fold the paper in the center so that one-half exactly covers the other; next fold the short, straight side over, so that both straight sides shall be of the same length. Additional security against leakage will be obtained if the strip last folded is again folded upon itself, preferably toward the inside.

In order to strengthen the weakest point of the cone, a smaller round filter may be placed on the outside of the larger filter and

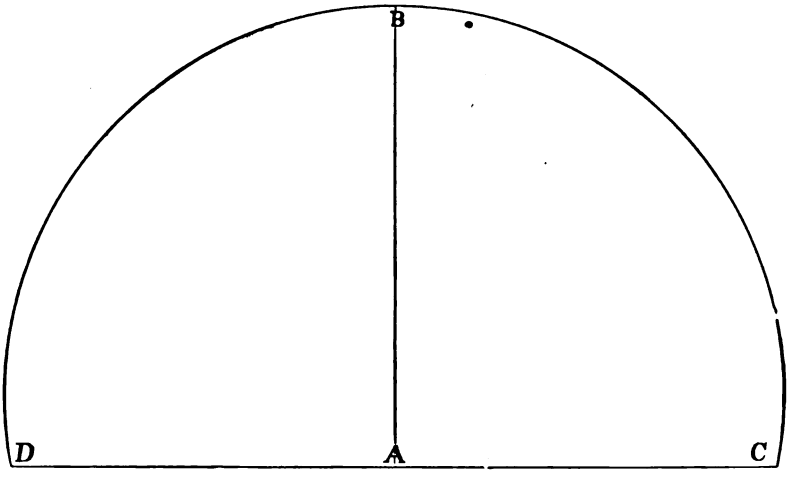


FIG. 127.—Diagram for making an economical plain filter, according to E. Classen's directions.

folded with the same; or one plain filter may be placed inside of another, so that even thicknesses of paper shall be on all sides.

The construction of a plaited filter is more readily demonstrated than explained; the simplest plan is to proceed as follows: Fold a

circular piece of filtering paper twice, after the manner directed above for a plain filter; this gives creases AB, AC, and AD (see Fig. 128).

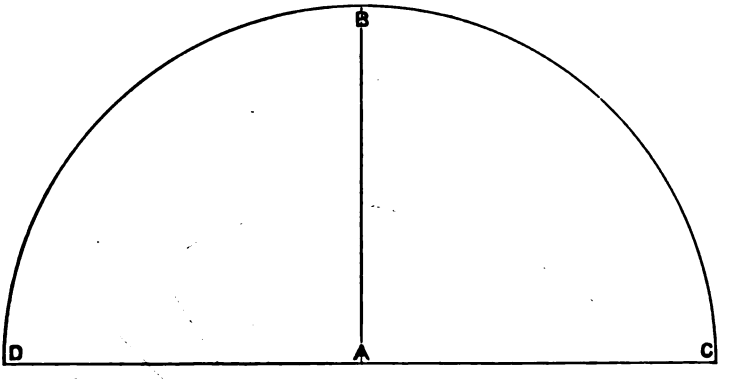


Fig. 128.

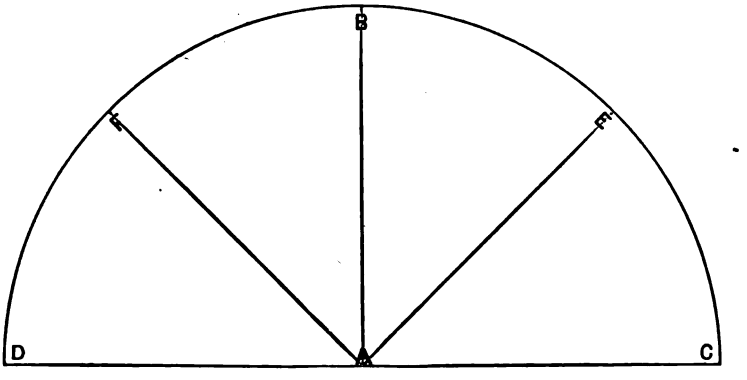


Fig. 129.

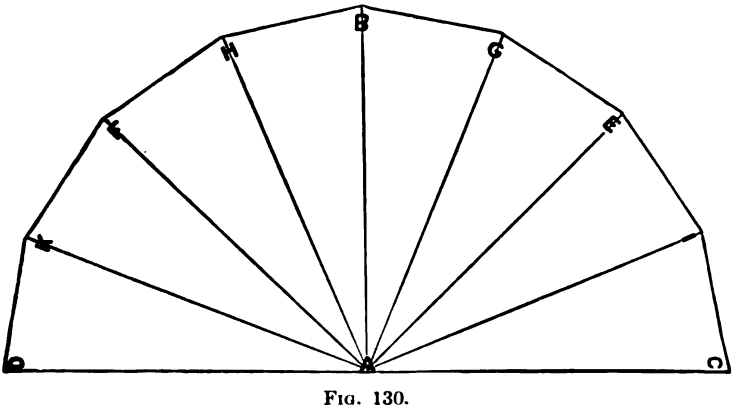


Fig. 130.

Next fold the crease *AC* over on *AB*, and the crease *AD* over on *AB;* this causes the creases *AE* and *AF* (see Fig. 129).

Now fold the crease *AC* over on *AF*, the crease *AD* over on *AE*, the crease *AC* over on *AE*, and the crease *AD* over on *AF;* this causes the creases *AG*, *AH*, *AI*, and *AK* (see Fig. 130).

The semicircle is now divided into 8 sectors, all creases being in the same direction; to complete the filter it is necessary to divide each sector into two by making a crease in a direction opposite to those already made—thus (see Fig. 131):

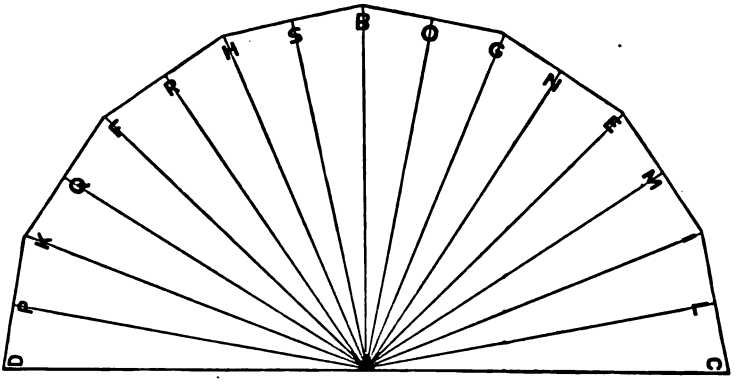


FIG. 131.—Showing the creases of a plaited filter.

Fold the	triangle	ACI	back	upon	itself;	this	causes the	crease AL.
"	"	AIE	"	"	"	"	"	AM.
"	"	AEG	"	"	"	"	"	AN.
"	"	AGB	"	"	"	"	"	AO.
"	"	ADK	"	"	"	"	"	AP.
"	"	AKF	"	"	"	"	"	AQ.
"	"	AFH	"	"	"	"	"	AR.
"	"	AHB	"	"	"	"	"	AS.

If the filter now be opened, it will be found divided into 32 sectors, 2 of which, *ACL* and *ADP*, opposite each other show both edges pointing in the same direction (see Fig. 132); to prevent these 2 sectors from lying flat against the glass when the filter is placed in the funnel, they should be again divided by placing the index finger in the center and bringing the edges up with the thumb and second finger, thus forming two new creases inward, *AU* and *AV* (see Fig. 132). In plaiting a filter, care must be observed that the creases be not pressed too firmly down to the very point, as this has a tendency to rupture the paper, or at least to weaken it materially. The plaited filter, when completed and ready for use, is divided into 34 sectors, and appears as shown in Fig. 134.

The points of paper filters may be toughened or strengthened by dipping them into strong nitric acid of 1.42 sp. gr., and then washing well with water to remove excess of acid; while a similar treatment

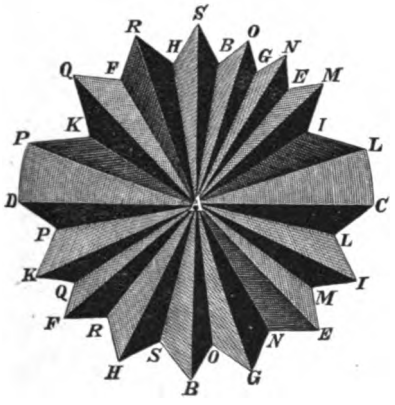


FIG. 132.

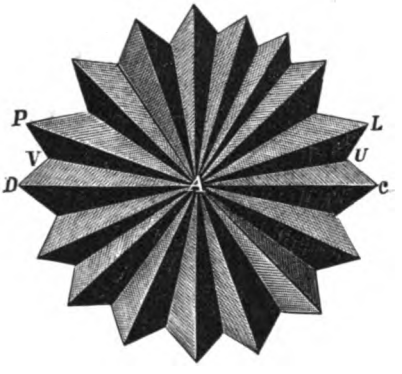


FIG. 133.

with sulphuric acid converts unsized paper into parchment paper, which is impervious to water. Nitric acid simply toughens the paper, but in no wise interferes with the absorption and passage of fluids through it, though its power of resistance is increased tenfold by this treatment.

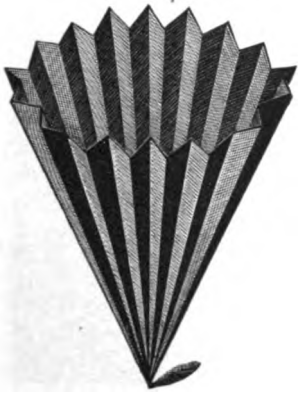


FIG. 134.—A complete plaited filter.

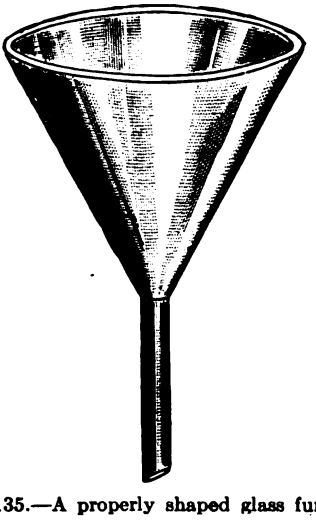


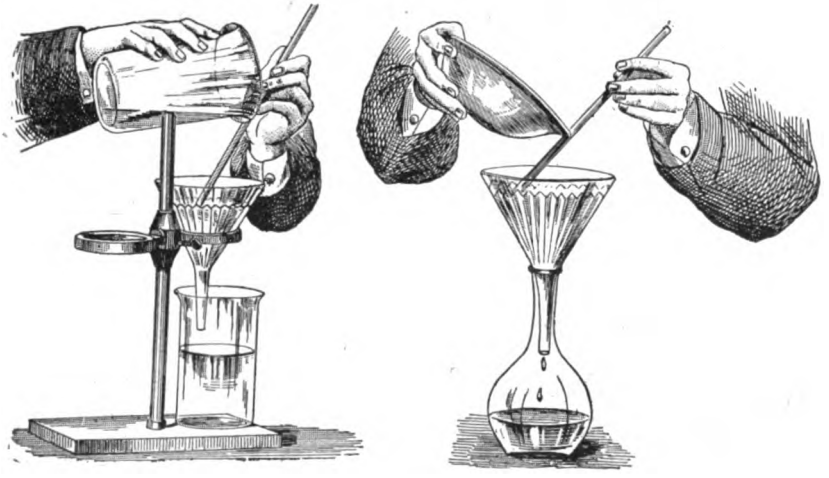
FIG. 135.—A properly shaped glass funnel.

When the object of filtration is to obtain a clear fluid irrespective of the solid matter removed, a plaited filter is always to be preferred to a plain one, as it exposes the entire surface of the paper to the liquid and allows the latter to pass through very rapidly.

Glass, porcelain, or metallic funnels, intended as supports for paper filters, should be of the shape shown in Fig. 135, having straight sides at an angle of 60 degrees to each other, and the end of the tube cut off obliquely, so as to compel the liquid to flow from one point only; when used over a jar or beaker it is well to place the lower end of the funnel in contact with the side of the vessel, thus preventing any annoyance from splashing of the liquid. In order to provide for the necessary escape of air from the receiving vessel, whenever a funnel is placed in a bottle a piece of twine or a strip of paper should be placed between the neck of the bottle and the tube of the funnel, the end of which should invariably project below the neck of the bottle.

When a paper filter is placed in a funnel, its upper edges should never quite reach to the rim of the funnel (better ½ inch below), so

FIG. 136. FIG. 137.



FIGS. 136 and 137.—Manner of pouring liquids into a filter with the aid of a guiding-rod.

as to allow the funnel to be covered with a piece of glass or of sheet rubber, for the purpose of keeping out dust and preventing evaporation; besides, if the filter projects beyond the funnel, considerable liquid will be drawn to the upper edges, owing to the capillarity of the paper, and evaporated, thus entailing a loss. In pouring a liquid into a filter, it should never be allowed to fall in a stream upon the apex or point, which is likely to break from the sudden force, but should be directed against the side by means of a guiding-rod, as shown in Figs. 136 and 137.

To insure a continuous supply of liquid to the filter, a bottle containing the fluid may be inverted over the funnel in the manner shown in Fig. 115, for supplying the menstruum to a percolator.

In manufacturing establishments where it is frequently necessary

to filter large quantities of liquids, such as elixirs, syrups, etc., use is made of horizontal and vertical filter presses, such as shown in Figs.

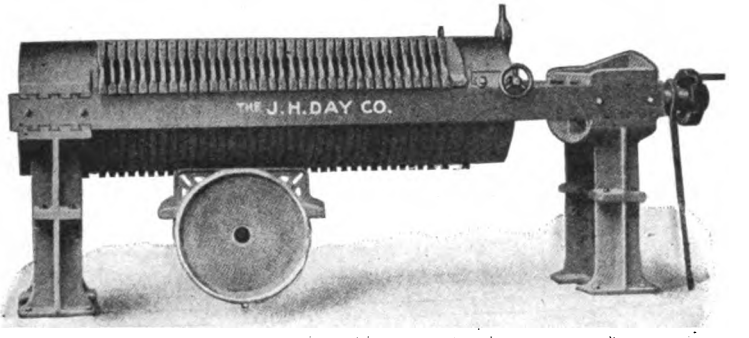


FIG. 138.—Horizontal filter press.

138 and 139. The filtering column consists of a series of heavy plates finely perforated, which are covered with paper pulp or square sheets of filter paper or felt, and varying from 6 to 12 inches in diameter. In the horizontal filter presses the liquid to be filtered is pumped through a central opening in the head plate, while in the vertical presses the liquid is generally forced through the filtering medium by gravity. The filtering surface of these machines is perfect and filtration can be carried on rapidly and thoroughly, the filtrate passing out perfectly clear in form of a solid stream. In the round vertical presses paper pulp is used altogether as a filtering medium, a layer of from $\frac{1}{4}$ to $\frac{5}{8}$ inch in thickness being provided on each plate, while in the horizontal and square vertical machines sheets or filter paper or felt are laid over the plates. These filter presses are made in different sizes, depending on the number of plates to be used; the vertical press shown in Fig. 139 being the product of the Karl Kiefer Machine Co., of Cincinnati, O., and the horizontal press (Fig. 138) of the J. H. Day Co., also of Cincinnati.

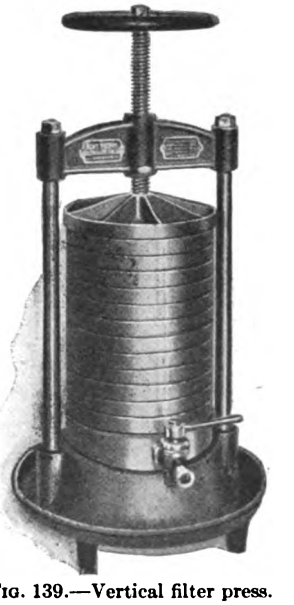


FIG. 139.—Vertical filter press.

For filtration of very volatile liquids, a glass tube, bent as in Fig. 140, may be placed under the filter against the side of the funnel; the twisted end will prevent the tube from slipping down, and air from the receiving bottle can readily pass up through the tube, which should

reach a little above the paper filter. The funnel, which should pass air-tight through a cork, must also be closed hermetically at the top.

Fig. 140.—Glass tube with twisted end.

Occasionally the filtration of substances which are not fluid at ordinary temperature becomes necessary, such as mutton suet, wax, petrolatum, ointments, etc.; this can be effected either by means of a hot-air funnel or a waterbath funnel. When hot air is to be used, the funnel containing a filter is suspended by means of porcelain strips, in a heavy tin jacket, which is surrounded by a copper cylinder, and heat is supplied from a circular low-power burner, as shown in Fig. 141, the heated air continually circulating around the funnel. The waterbath funnel consists of a glass funnel surrounded by a double tin or copper jacket, as shown in Fig. 142; the opening, *a*, at the top of the jacket is for the purpose of introducing hot water and the projecting tube, *c*, near the bottom, for maintaining the heat of the water by means of a spirit lamp or gas jet. The projecting rim, *e*, is intended to prevent any water, running over at *a*, from entering the bottle or vessel, in the mouth of which the neck of the funnel may be placed. The substance to be filtered should first be

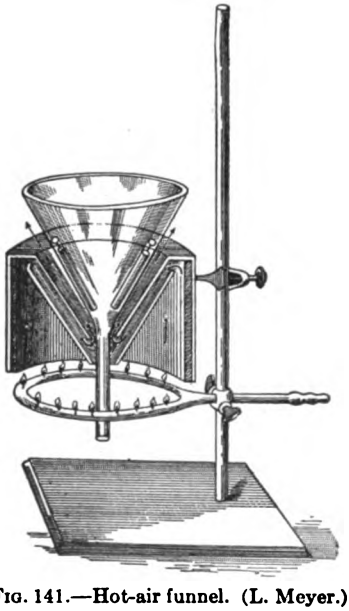


Fig. 141.—Hot-air funnel. (L. Meyer.)

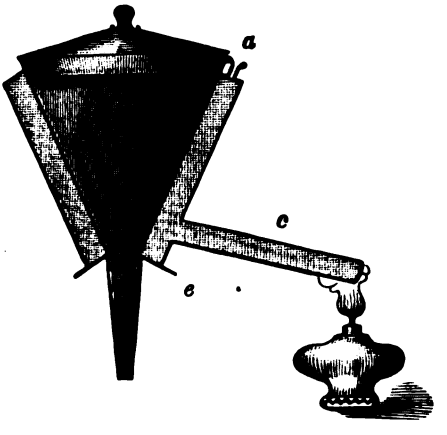


Fig. 142.—Sectional view of hot-water funnel with cover.

completely melted and then poured into the filter contained in the previously heated funnel, which must be kept covered to avoid loss of heat.

The rate of filtration of a liquid can be greatly increased by exhausting the air from the funnel tube and receiving bottle, thereby

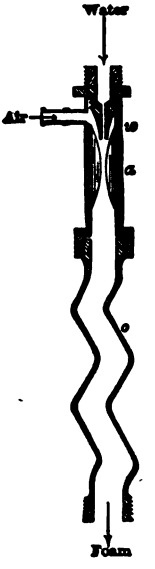


FIG. 143.—Richard's filter pump.

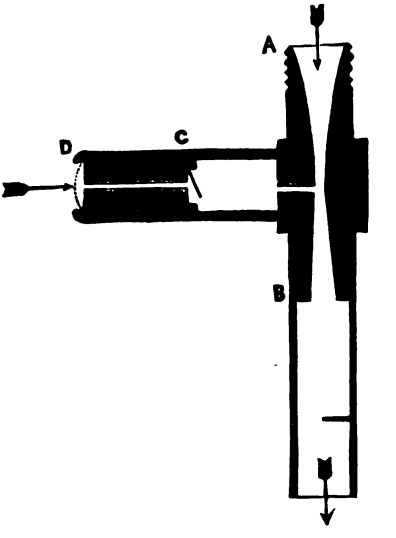


FIG. 144.—Chapman's filter pump.

increasing the atmospheric pressure above the liquid; the necessity for this operation occurs more frequently in the analyst's laboratory than with pharmacists, yet an acquaintance with the apparatus employed is desirable. The exhaustion of the air is effected by means of an

FIG. 145.—Geissler's glass filter pump.

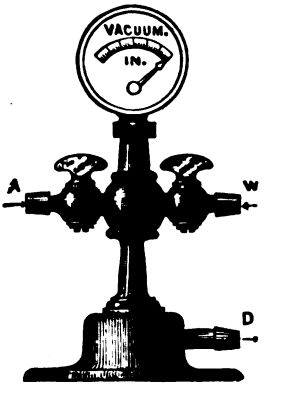


FIG. 146.—Portable filter pump, with manometer.

aspirator connected with a water supply and with the receiving bottle by rubber tubing. Figs. 143, 144, 145, and 146 represent

different styles of filter pumps; as seen in two of the illustrations, suction of air is produced by forcing water, under pressure, through a contracted space which communicates with the air to be aspirated. The internal construction of the pump shown in Fig. 146 is similar to that of the other two, but the water which enters at *W* is discharged at *D* on the side; hence this apparatus can be used at any desired point, being connected by means of tubing with the water supply and sink: with air-tight connections a nearly absolute vacuum can be obtained, as may be seen from the indications of the manometer attached to the top of the pump. Whenever filter pumps are used, the pressure on the liquid filtering becomes so great as to endanger the safety of the filter point; an extra support is therefore provided in the shape of a finely perforated platinum cone set in the throat of the funnel in which the paper cone is placed.

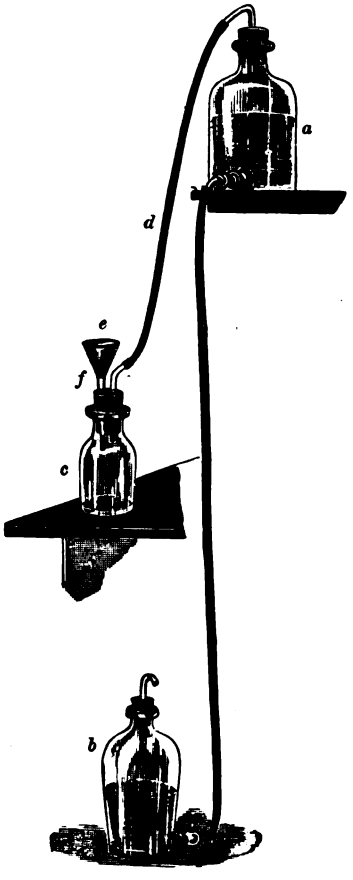


FIG. 147.—Filtering apparatus: *a* and *b* are two large bottles connected, as indicated in the drawing, by a narrow India-rubber tube with thick walls. The upper bottle should be placed as high as possible. *c* is a bottle into which the filtrate is to pass. The interior of this is in connection with *a* by a thick-walled tube, *d*. Into the stopper of *c* the funnel *e* is fixed, and at its apex lies a small perforated platinum cone, *f*, which supports the apex of the filter when the interior of *c* is partially exhausted by the discharge of the water in *a* into *b*.

When an aspirator or filter pump is used in connection with water drawn from the city supply, a very annoying accident sometimes happens when the water pressure is suddenly reduced, or when the pump is cut off, namely, a portion of water is drawn up into the vessel from which the air is being aspirated; this can be guarded against by interposing another vessel between the pump and the aspirated vessel.

For rarefying the air under filters when water pressure is not available a simpler contrivance may be resorted to, as shown in Fig. 147; the water flowing from the upper to the lower bottle withdraws air from the receiving flask, and by simply changing the bottles when the upper one becomes empty the operation may be continued for any length of time, the air-tube being closed by means of a pinchcock while the

bottles are being changed. Ordinary 5-gallon castor oil cans may be conveniently used in place of bottles.

The turbidity of some liquids is caused by suspension of matter in so finely divided a form that its removal cannot be effected by the ordinary methods of filtration, and recourse must be had to the interposition of some other substance to render the liquid perfectly transparent and clear; in such cases paper pulp, purified infusorial earth or kieselguhr, and purified talc form excellent filtering media. Paper pulp is readily prepared from scraps of filtering paper by treating them with hot water in a mortar or with active agitation in a bottle. When the paper has become thoroughly pulped the excessive moisture may be removed by expression in a clean cloth, after which the pulp

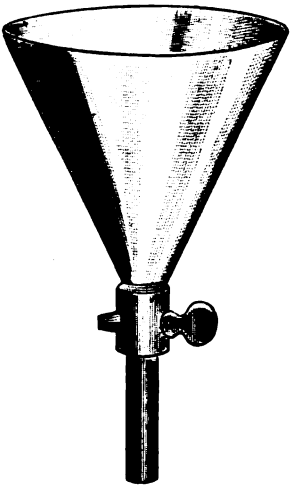


FIG. 148.—Glass separator (funnel shape).

FIG. 149.—Glass separator (globe shape).

may be added to the liquid to be filtered and thoroughly incorporated by agitation. The finely divided pulp forms a layer on the surface of the filter which effectually prevents the passage of minute particles of insoluble matter by absorbing these into its own fiber. For acid liquids, finely shredded asbestos is preferable.

Immiscible liquids can be conveniently separated from each other by pouring the mixture into specially constructed apparatus known as separators or separatory funnels (see Figs. 148 and 149), and after the liquids have separated into distinct layers by reason of their different specific gravities, withdrawing the lower liquid by carefully opening the stopcock in the tube and allowing it to flow into a suitable receiving vessel.

DECANTATION.

Decantation, or the process of pouring a fluid gently from one vessel to another, is employed in pharmacy more particularly in connection with the washing of precipitates; sometimes it is resorted to for the separation of immiscible liquids, but separation in such a case can never be so complete as by the method explained above.

All precipitates when freshly obtained by double decomposition of two soluble substances, are more or less contaminated with a solution of the other newly formed salt; to remove such impurities the process of washing, which consists in treating the precipitate repeatedly with fresh portions of water, is employed. Thus, when solutions of lead nitrate and potassium iodide are mixed, the newly formed lead iodide is deposited while potassium nitrate remains in solution, and must be

FIG. 150.—Decantation with aid of a glass rod.

removed before the precipitate can be dried. The thorough washing of precipitates is a very important operation, which may be performed by continued treatment with water on filters and cloth strainers, or by allowing the liquid in which the precipitate was formed to settle completely in suitable vessels, decanting the clear supernatant fluid, adding successive portions of fresh water, and again decanting after each settlement; it is essential that the fresh water and precipitate be well mixed by stirring or agitation after each addition.

The decantation of a fluid is not always so simple an operation as it may seem; the shape and size of the vessel from which the liquid is to be poured, the nature of the liquid and the height to which it fills the vessel, all influence the flow of the liquid. When the fluid to be decanted is water or an aqueous solution, and the vessel is not very large, either with or without a lip, the simplest plan is to transfer

the liquid with the aid of a glass rod, as shown in Fig. 150. The guiding rod prevents the splitting of the current of the liquid, to which is due the well known phenomenon of liquids running back on the sides of the vessel from which they are poured. When the vessel from which the liquid is to be poured is too large or too full of liquid

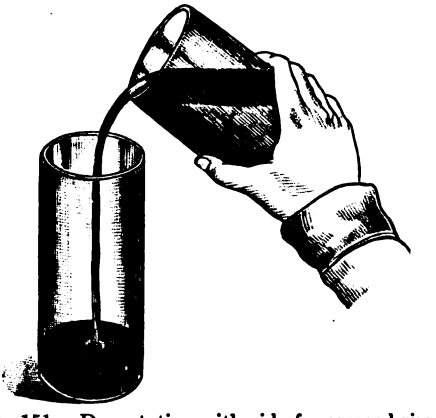


FIG. 151.—Decantation with aid of a greased rim.

to admit of decantation with the aid of a glass rod, the liquid may be made to flow in a somewhat contracted but solid stream by greasing the rim of the vessel with a little rosin cerate, which prevents adhesion of the liquid to the glass and enables the force of cohesion to keep the particles of liquid united; Fig. 151 illustrates the operation.

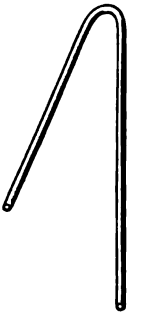


FIG. 152.—Plain siphon.

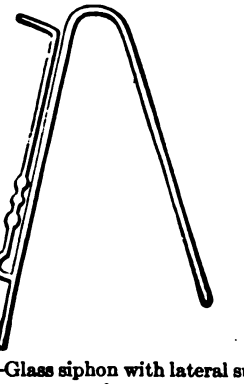


FIG. 153.—Glass siphon with lateral suction tube.

Sometimes an instrument called a *siphon* is employed to draw off the supernatant liquid from a precipitate, the method being particularly desirable if the precipitate is light and easily disturbed by handling the vessel; the simple construction of a siphon is shown in Figs. 152 and 153. The two limbs of the glass tube are of unequal

length, the shorter one being immersed in the liquid; it is manifest that if the air be entirely withdrawn from the tube by suction, the liquid will rise and fill the tube, owing to the pressure of the atmosphere on the surface of the liquid. The flow of the liquid, having been started, will continue by reason of its downward tendency or gravitation aided by atmospheric pressure, until the liquid falls below the mouth of the shorter limb, or until it rises in the receiving vessel to the level of the liquid in the vessel from which it flows. A plain rubber tube may often be used with advantage as a siphon, remembering that the end of the tubing out of the liquid should always reach lower than that in the liquid, so as to insure a continuous flow.

CLARIFICATION.

Clarification is a process of separation designed to render cloudy or turbid liquids transparent by means other than those thus far considered; it is generally effected through the agency of heat; in every instance, however, the separated disturbing element must subsequently be removed by filtration or decantation. The viscid character of some liquids renders the various methods of filtration impracticable; whereas the mere application of heat, by increasing their fluidity, enables the suspended particles of solid matter to separate spontaneously, some rising to the surface while others sink to the bottom; if the liquid be allowed to remain at perfect rest while separation is going on, the lighter particles will form a layer, which can often be completely removed with the aid of a skimmer, while the heavy sedimentary matter is readily retained on a cloth strainer. Honey and balsam of fir may be treated in this manner. Saline solutions concentrated for the purpose of crystallization are frequently contaminated with dust and other foreign matter which passes freely through cloth and paper filters; they may be readily clarified by adding paper pulp (see page 173), which effectually removes the fine particles of dirt from the boiling liquid, by enveloping them in its own fiber and retaining them on the strainer.

Other substances added to turbid liquids in order to effect clarification are egg albumen, gelatin, and milk. White of egg, or albumen possesses the property of coagulating or solidifying when heated to about 80° C. (176° F.), therefore when it is added to liquids and then heated, any solid matter impairing the transparency of the liquids will be enclosed in the coagulum formed, and can then be removed by straining; some vegetable solutions prepared with cold aqueous menstrua contain albuminous matter originally present in the drug, which, upon heating to the boiling point, is coagulated, and is thus gotten rid of, as in the case of extract of gentian. Albumen is preferably mixed with a little water before adding it to the liquid to be clarified, and then thoroughly incorporated with it before heating.

Since albumen forms insoluble compounds with some plant constituents, it must be judiciously employed, lest the active principles contained in a liquid be removed by it. When the turbidity of a liquid is due to tannin, gelatin is generally preferred as a clarifying agent it is used like albumen, and forms insoluble tannate of gelatin, or leather. Milk is especially adapted to clarifying acid liquids, as the casein of the milk is coagulated by the acid, and thus the impurities are removed by becoming enveloped in the coagulum.

Clarification of liquids may also be effected by subsidence and fermentation; the former is often applied to fixed oils, which are allowed to remain undisturbed in tightly closed containers for some time, so that albuminous and mucilaginous matter derived from the seed may gradually separate and settle to the bottom. Fruit juices, as a rule, contain certain principles which tend to render them cloudy and unsightly, but which can be removed by fermentation at a moderate temperature, about 20° C. (68° F.); the matter thus separated settles to the bottom and the clear liquid may be drawn off by means of a siphon or otherwise.

DECOLORATION.

Decoloration, as the name indicates, is a process for the removal of color from liquids, and is practised on a large scale in sugar refineries. For pharmaceutical purposes it is chiefly confined to solutions of organic acids, alkaloids, and neutral principles. The most effective decolorizing agent is animal charcoal, made either from bone or blood; ordinary bone black requires purification by means of hot hydrochloric acid, whereby certain lime salts are removed. Animal charcoal is perferably used in a granular condition, and its utility as a decolorizer depends upon its porosity; unfortunately, charcoal absorbs also other matters held in solution besides color, and this may occasion loss of valuable constituents unless the charcoal is subsequently washed with fresh menstruum. The usual method of employing animal charcoal is either by digesting it with the liquid to be decolorized, or by allowing the latter to percolate slowly through a column of the charcoal; in the former case the liquid requires subsequent filtration.

EXPRESSION.

Expression is a process of separation which requires the exercise of more or less force, since it is employed in those cases where the amount of liquid is small compared with the quantity of solid matter to be removed; as, for instance, in the preparation of fruit juices, the expression of macerated drugs, or the recovery of menstruum that may have been retained by the marc in percolation when water fails to force it through. For the purposes of the pharmacist, the tincture press, Fig. 154, and the Enterprise press, Fig. 155, will be

found very serviceable; in the former the substance to be expressed, having been put into a suitable canvas or press-cloth bag, is placed on a perforated disk in a porcelain-lined iron cylinder, pressure being produced by means of a lever screw bearing upon a plate on top of the

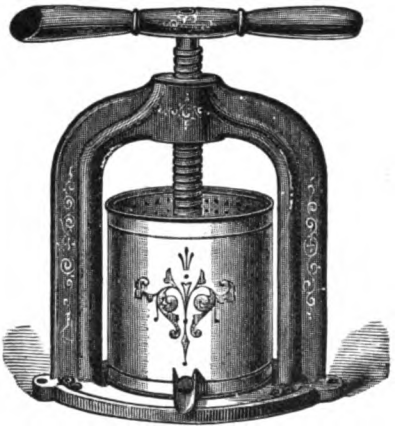


FIG. 154.—Tincture press (vertical).

bag. The expressed liquid flows out through the lip attached to the cylinder. The Enterprise press is operated without the use of press-cloths, the material to be expressed being fed directly into the hopper communicating with a tapering cylinder containing a large screw, the thread of which gradually diminishes in size toward the smaller end; the cylinder is provided with a perforated plate in the bottom,

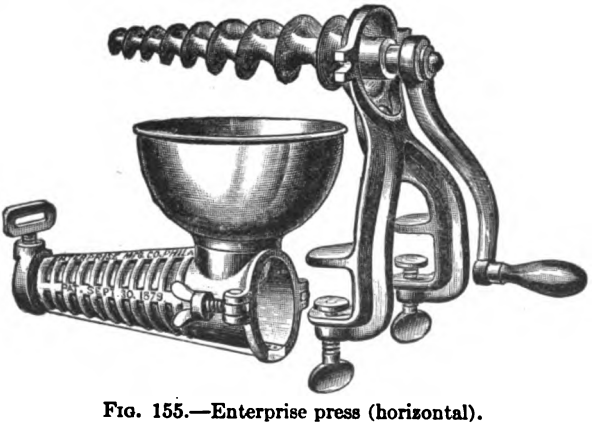


FIG. 155.—Enterprise press (horizontal).

and the material is compressed by means of the tapering screw, which is turned with a crank. The dry residue is discharged through an opening in the small end of the cylinder, and the liquid expressed flows out through the perforated plate.

Another method of separation is that effected by means of centrifugal machines, which are extensively employed in manufacturing establishments for washing and drying crystals as well as for the rapid withdrawal of moisture in the drying of certain precipitates and

FIG. 156.—Centrifugal separator (for hand use).

fabrics. The apparatus used consists of a metal drum or cylinder having a solid bottom but open at the top, and provided with perforated sides, which revolves on its own axis inside of a larger stationary cylinder supplied with a cover to keep out dust, and an outlet tube

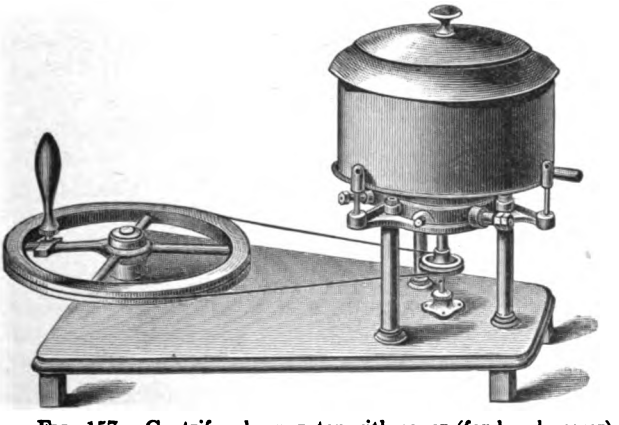


FIG. 157.—Centrifugal separator with cover (for hand power).

at the bottom, through which the liquid coming from the inner cylinder is allowed to flow out; sometimes the perforated sides of the inner cylinder are covered with bolting cloth, according to the substance to be operated upon, and the rotary motion is imparted to the cylinder

from below by means of steam power. The value of centrifugal machines depends upon the velocity with which the material to be centrifugalized is hurled around and against the perforated sides, the revolutions usually numbering as high as 2000 or 3000 and even more per minute; the strong draft of air created between the walls of the inner and outer cylinders by such rapid revolution effects drying of the material more thoroughly than is possible by expression or other means. The use of centrifugal machines is based on the well-known laws of motion and inertia, according to which a body put in motion continues in a straight line unless turned from its path by some external force, and thus liquids can readily be separated from solids when a mixture of the two is dashed against a finely perforated surface. In sugar refineries centrifugalizing is the only suitable method known for separating the granulated sugar from the viscid mother liquor or molasses.

For special use in the pharmacist's laboratory, small centrifugal machines, to be operated by hand, have been devised; the outer cylinder is usually made of enamelled iron, while the inner perforated cylinder is made of porcelain; those in which motion is supplied from above are frequently provided with a cover for the inner cylinder, while in those operated from below a cover is fitted to the outer cylinder. Figs. 156 and 157 are shown two styles of hand-power machines.

DIALYSIS.

Dialysis is a process of separation which differs entirely from those considered thus far, in not aiming at the removal of insoluble matter suspended in a liquid, but at bringing about a separation between solvents and matter held by them in solution; also between different kinds of matter held in solution by the same solvent. It is a practical application of the principle of osmosis, and is due solely to surface action and the difference in diffusibility of various substances. The word dialysis is derived from the Greek *διαλύειν*, to part asunder, to lose one from another, and was applied by Prof. Graham, of England, to the method of separation devised by him in 1861. The process consists in placing a solution of the substances to be separated on a porous diaphragm and suspending this in pure water; osmosis is established, and certain substances will pass through the diaphragm into solution in the water, while others will remain on the diaphragm, the rapidity of diffusion being in proportion to the strength of the solution and increasing with the rise in temperature. Graham discovered that crystallizable substances passed through the diaphragm freely, while amorphous bodies, such as gums, starch, gelatin, etc., either did not diffuse at all, or only very slowly; he applied the name *crystalloid* (resembling crystals) to all substances thus capable of diffusion through a septum, and the name *colloid* (resembling glue or jelly) to those substances remaining on the diaphragm. All colloids

are amorphous or non-crystallizable, but all crystalloids are not necessarily capable of crystallization, as, for instance, hydrochloric acid, the most highly diffusible body, and many others. By means of dialysis, sugar can be readily separated from gum or starch, pepsin from peptones, iron salts from iron oxide, etc. Thus the process has become most valuable to manufacturers, while the analyst often finds dialysis the only means for determining the presence of certain substances in complex vegetable solutions, as, for instance, arsenous acid, corrosive mercuric chloride, or potassium iodide in compound sarsaparilla mixtures and other proprietary medicines, where the dark color and complex nature of the solution preclude all other methods of separation.

The apparatus used for dialysis is of very simple construction, as shown in Figs. 158 and 159. It consists of a circular glass vessel, with flat bottom and of convenient size, also another smaller circular but bottomless vessel of hard rubber or glass, having a projecting rim, over which is stretched a piece of bladder, parchment, or parchment paper (see page 167). The latter constitutes the dialyser proper,

FIG. 158.

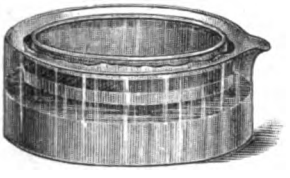
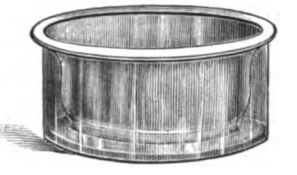


FIG. 159.



Glass dialysers.

and into it is poured the solution to be dialysed, to the depth of about $\frac{1}{2}$ or $\frac{3}{4}$ inch, after which it is floated in distilled water contained in the other larger vessel. In Fig. 159 the glass dialyser is provided at the top with a broad rim which rests upon the edge of the outer vessel, and thus serves as a cover to protect the water against dust, etc. In place of the foregoing convenient apparatus, an ordinary clean hog or beef bladder may be used; the same should be three-fourths filled with the solution, and then suspended in a large vessel of water.

Diffusion in a dialyser will not take place unless the porous membrane or septum is in contact with water; and, moreover, its limit will be reached when the water on the outside becomes charged with such a quantity of crystalloids as to render the strength of the solution identical with that in the dialyser; hence it is necessary that the quantity of water in the outer vessel be much greater than that of the liquid in the dialyser, and that it be renewed from time to time. The crystalloids from a 10 per cent. solution of sugar, salt, or hydrochloric acid will readily diffuse through a septum if the latter is placed in contact with water, but no diffusion whatever will take place if the dialyser be floated in a 10 per cent. solution of the same substances.

While the rate of diffusion varies greatly for different substances, it was found by Graham to be uniform for isomorphous bodies—that is those having exactly the same crystalline form.

The colloidal residue remaining on the diaphragm is termed the *dialysate*, while the solution of the crystalloids that have passed through the membrane is known as the *diffusate*.

STERILIZATION.

This process, which derives its name from the Latin word *sterilis*, meaning unproductive, consists in destroying microörganisms or bacteria derived from germs ever present in the air and found in glass, metal, and porcelain vessels and their contents, by exposing the apparatus and contents to a temperature which is fatal to such microorganisms, usually from 100° to 170° C. (212°–338° F.). By this means many preparations are rendered more permanent, and all possible danger of infection from the use of non-sterilized liquids is averted.

Directions for preparing the sterile solutions are given in the Chapter on Solutions, on page 140. Surgical dressings, such as cotton, bandages, gauzes, ligatures, etc., may be rendered sterile by treatment with steam in a pressure apparatus or autoclave (see Fig. 101) at 115° C. for fifteen minutes or by exposure to dry heat in an ordinary airbath or sterilizer at a temperature of from 160° to 170° C. for two hours. It should be remembered that all surgical materials are not amenable to such thorough treatment without more or less deterioration taking place. Bandages must be folded or packed in such a manner as to permit the penetration of steam or dry heat during the process and should be so arranged that after the sterilization is completed all subsequent contamination with bacteria will be prevented. This is usually accomplished by immediately enclosing them in glass containers or wrapping them in a number of thicknesses of previously sterilized parchment paper.

Powders of all kinds, if not decomposed or volatilized by application of heat, can be sterilized in a hot-air oven at a temperature of 160° to 170° C.

Pasteurization.—Pasteurization, so named in honor of Louis Pasteur, the famous French bacteriologist and chemist, differs from sterilization chiefly in the lower degree of heat employed. The object of pasteurization is to destroy certain spores in liquids and to check or prevent fermentation. It consists in heating the liquid to be pasteurized to a temperature of 60° to 70° C. (140°–158° F.) for thirty minutes, in some cases on two or three consecutive days, and then preventing the further access of spores by closing the vessel with a pledget of sterile cotton.

CHAPTER X.

SEPARATION OF VOLATILE MATTER.

ADVANTAGE may be taken of the volatility of some substances for the purpose of separation, and by their vaporization either of the following objects may be attained:

1. The separation of a volatile liquid from a solid, with a view to retain the solid substance, or of one liquid from another, to obtain the less volatile; in such cases the process is termed *evaporation.*

2. When the separation of liquid and solid substances, by means of evaporation, is carried to complete dryness, the process is more particularly designated as *desiccation* or *exsiccation.*

3. The separation of a volatile liquid from either a less volatile liquid or a solid, in order to obtain and preserve the volatilized liquid for future use; the process is then known as *distillation.*

4. The separation of a volatile solid from either a liquid or a solid which is more fixed, the object sought being the volatilized solid body; this process is termed *sublimation.*

EVAPORATION.

In the practice of pharmacy evaporation is extensively resorted to for the concentration of vegetable and saline solutions, the latter with a special view to subsequent crystallization, and the laws which control the process should be well understood. Evaporation may be divided into four kinds, namely, evaporation over a naked fire, on a waterbath or steambath, in a vacuum apparatus, and spontaneous evaporation. Evaporation over a naked fire is effected by the direct radiation of heat from a fire, on the bottom of an uncovered dish or pan, and is available when the substance in solution is not injured by direct heat or high temperature; it is usually employed for the concentration of saline solutions for crystallization, but only when the liquid to be vaporized is water. When evaporation at temperatures below that of boiling water is desired, the low-temperature burner shown on page 88 may be used with advantage, by means of which continuous currents of hot air may be made to heat the bottom and sides of the dish, and yet actual contact of the latter with the flame be avoided.

Evaporation on a waterbath or steambath is the method most frequently resorted to; the latter can also be employed for rapid concentration of solutions at a high temperature without the danger of injury from direct heat of the fire. Evaporation at temperatures below 100°

C. (212° F.) is effected on a waterbath, and is confined to the surface of the liquid; this is the method chosen for the concentration of vegetable and other solutions liable to be injured by heat at or above that of boiling water and when more volatile solvents than water are present. Whenever a liquid is to be evaporated at a temperature below its boiling point, rapidity of evaporation will depend upon the extent of surface exposed to the air, since the formation of vapor takes place only at the surface; hence broad, shallow vessels are to be preferred. During the boiling of liquids the rate of evaporation depends (the source of heat being constant) entirely upon the extent of surface to which heat is applied, since the more numerous the points of contact of the vessel with the source of heat the more rapid must be the formation of vapor, and ebullition is but the phenomenon of the rapid disengagement of vapor from the interior of a liquid.

Evaporation *in vacuo*, being conducted under greatly reduced pressure, is admirably adapted to the concentration of liquids holding vegetable matter in solution, but is employed only in large manufacturing establishments, owing to the complicated and expensive apparatus necessary for the operation; the process insures rapid evaporation at a low temperature, without the possibility of injury from contact with the air. In sugar refineries weak saccharine solutions are rapidly concentrated in vacuum pans to avoid coloration and inversion of the sugar. For the preparation of fluid and solid extracts, concentration *in vacuo* offers advantages not obtainable by any other method, as a low temperature and complete exclusion of air insure the retention of soluble matter in its original form as extracted from the drug. The effect of evaporation in a vacuum apparatus is readily seen in the great change produced in the boiling point of water under such conditions. Thus, ordinarily, when the atmospheric pressure is 30 inches, water boils at 100° C. (212° F.), whereas if the pressure be reduced one-half, that is, if a vacuum of 15 inches be produced, it will boil at 80° C. (176° F.); in a vacuum of 21.7 inches it will boil at 67° C. (152.6° F.), or at 52° C. (125.6° F.) in a vacuum of 25.85 inches, or at 37.78° C. (100° F.) in a vacuum of 28 inches, and even at 26.67° C. (80° F.) if a vacuum of 28.9 inches be maintained. The vacuum apparatus consists of an air-tight boiler connected with a steambath and an air-pump operated by machinery, for exhausting the air and vapor.

Spontaneous evaporation proceeds naturally, without the use of external force, and consists in allowing vaporization to take place at the ordinary temperature. It is due to diffusion of the vapor of the liquid into the surrounding atmosphere, and its rapidity depends upon the dryness and temperature of the air; the most effectual means of promoting it, therefore, is to allow a current of warm, dry air to pass over the surface of the evaporating liquid, as this will remove the superincumbent air as soon as diffusion into it has taken place.

The most desirable evaporating dishes for general use are those

known as Royal Berlin porcelain ware (see Fig. 160); they resist sudden changes in temperature better than other earthen vessels, and possess the great advantage of not being permeable by colored fluids. When used over the direct fire, a piece of wire gauze should be interposed between the flame and the dish, so as to distribute the heat more uniformly over the bottom of the vessel and prevent the flame from striking any particular point. As glass and porcelain vessels are liable to crack when suddenly brought in contact with a cold surface after having been heated, it will prove economical to place them on

FIG. 160.—Royal Berlin porcelain dish.

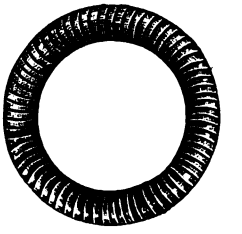


FIG. 161.—Straw ring for supporting dishes and flasks.

straw rings or rubber grommets (see Figs. 161 and 162) when hot; these also serve admirably as supports to prevent tilting of round-bottom dishes and flasks. Grommets are easily made by forming rubber tubing into a circle and uniting the ends by means of a wooden plug; three short pieces of similar tubing of larger size are then placed one over the joint and the others at equal distances apart, which arrangement permits a circulation of air around the bottom of the vessel. Enamelled cast-iron dishes are extensively used, but, owing to the non-uniform expansion and contraction of the metal and enamel,

FIG. 162.—Grommets.

the latter is apt to crack and chip off, unless heat be very carefully applied; the so-called "agateware" dishes are better, being made of sheet iron and then enamelled. For neutral liquids, well tinned copper pans may be employed; while for the evaporation of solutions of caustic soda or potassa, silver or perfectly clean iron vessels are necessary. Evaporation of liquids in open vessels is materially facilitated by keeping the liquid in motion, which in small operations can be readily done by stirring with a glass rod or porcelain spatula, and on a large scale by means of a mechanical stirrer operated by

steam or water power. A simple form of mechanical stirrer is shown in Fig. 163; it was devised by John Moss, of England, and consists of a $1\frac{1}{4}$ inch shaft, *A*, and a hollow shaft, *B*, which readily slides over it. These shafts are fastened together at *C*, by means of a pin, and are held vertically over the center of the evaporating pan by means of the brackets; *D*, attached to the wall. Power for turning the shaft is supplied by a band passing around the grooved pulley at *E*. To the lower end of *B* is attached a hard-wood block, on the opposite sides of which are fastened the stirring paddles, *F*, which can be set at any desired angle, by means of winged-screw bolts, as seen in the cut. The paddles, which are usually made of ash, may consist of solid blades, 2 feet long by $2\frac{1}{2}$ inches wide and $\frac{5}{8}$ inch thick, but are preferably perforated with holes not less than 1 inch in diameter, which prevent the contents of the pan from moving around as a solid mass, and insure the formation of currents of different sizes, moving at different rates of speed, whereby evaporation is greatly facilitated.

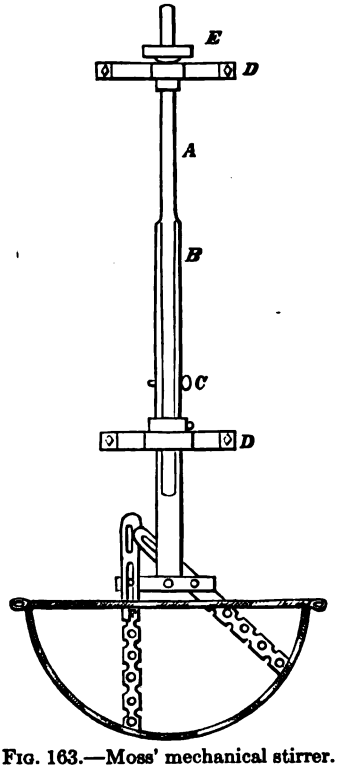


FIG. 163.—Moss' mechanical stirrer.

Corrosive vapors are sometimes given off during the evaporation of acid liquids; to prevent these from contaminating the atmosphere of the store or laboratory, and also to avoid saturating the air with moisture, evaporation may be conveniently conducted under a hood communicating with a flue. When evaporation is directed to be carried to a given weight, a tared dish must be used, the dish and contents being weighed from time to time until the desired weight has been reached. If evaporation is to be carried to a given volume, the simplest plan is to measure the desired volume of water into a dish standing on a level surface, then introduce into the center of the liquid a thin stick of wood and mark the height to which the water reaches —the liquid to be reduced in volume must be evaporated in this same dish until it stands at the point indicated by the notch on the stick.

DESICCATION.

Desiccation, or exsiccation, a process of drying completely, is another method of evaporation, and is employed for driving off the

moisture from vegetable drugs, crystalline salts, precipitates pills, tablets, lozenges, etc. The temperature for effecting desiccation may vary from 40° C. (104° F.) to 200° C. (392° F.), the heating being carried on either in the open air on sandbaths or in closed compart-

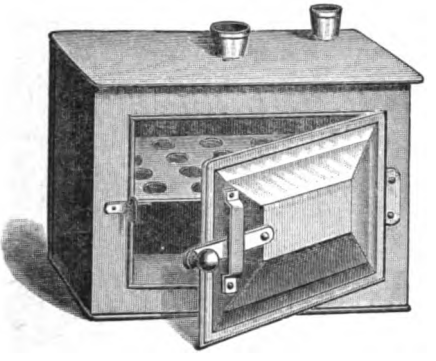


FIG. 164.—Hot-water drying oven.

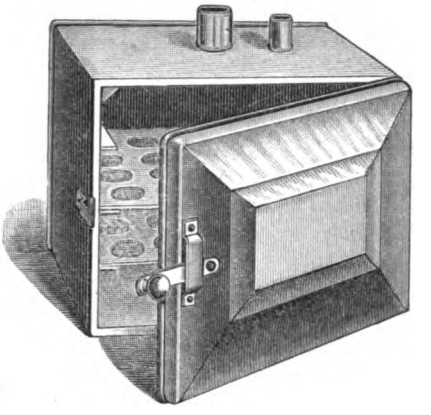


FIG. 165.—Hot-air drying oven.

ments. For small operations, and when heat not higher than 100° C. (212° F.) is required, a portable water oven (Fig. 164) will answer admirably. This consists of a double-walled copper box containing water, which may be heated to boiling, and thus heat supplied to the interior compartment, which is provided with a perforated tray, a closely fitting door, and an opening in the top for the escape of moisture. For temperatures above 100° C. (212° F.) a hot-air bath (Fig. 165) may be employed. This consists of a single-walled copper box through which heated air is constantly circulating, and which is provided with a thermometer through an opening in the top. In large manufacturing establishments desiccation is carried on in appropriate drying closets built of kiln-dried wood and heated by coils of steam pipe.

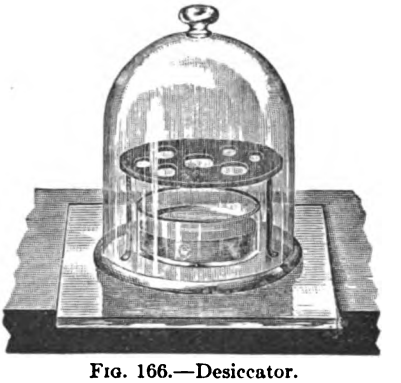


FIG. 166.—Desiccator.

The term exsiccation in pharmacy is usually reserved for a process of evaporation in which crystalline salts are first moderately heated to efflorescence, and then with constant stirring more strongly until all or most of the water of crystallization has been expelled and the powder has ceased losing weight. Dried alum, dried sulphate of iron, and dried sulphate of copper are prepared by exsiccation. Exsiccated

or anhydrous salts may be restored to their original composition by simple solution in water.

Desiccator is the name applied to glass apparatus of varied construction, in which substances, after having been completely dried by heat, are allowed to cool in air which is kept entirely free from moisture by strong sulphuric acid, fused calcium cloride or freshly burned lime, placed in the lower cup of the apparatus. Sometimes the desiccator is also used to abstract moisture from material which, owing to its volatile nature, cannot be exposed to heat without loss or injury, and since sulphuric acid and lime both have a great affinity for water, perfect desiccation can thus be effected. Fig. 166 represents one of the styles of this very useful apparatus, which is indispensable in quantitative chemical analysis.

INCINERATION, CALCINATION, AND TORREFACTION.

Incineration, or reduction to ash, is a process of separation applied to vegetable matter, which consists in heating it to redness in open vessels, with full access of air, until all carbon has been consumed or converted into carbon dioxide.

Calcination differs from incineration chiefly in being applied to mineral substances, which are heated to redness without fusion, for the purpose of expelling some volatile constituent at a high heat, as the carbonic acid from magnesium and calcium carbonates in the preparation of magnesia (calcined) and unslaked lime, or the nitric acid from mercuric and cupric nitrates in the preparation of the respective oxides.

Torrefaction, or roasting, is not so much a method of separation as one which is intended to modify the properties of substances by exposing them to dry heat to a point short of carbonization. Roasted coffee is probably the most familiar example. Fifty or sixty years ago physicians used rhubarb, dried, and roasted in very coarse powder, which had thus lost its cathartic properties, but had retained its astringency.

DISTILLATION.

Distillation differs from evaporation chiefly in the utilization of the volatilized liquid, and in order, therefore, that no loss may occur, the process must be conducted in certain closed apparatus in which condensation of the vaporized liquid may be effected. As the application of heat to a liquid is necessary to convert it into vapor, so inversely the withdrawal of heat from vapor is essential to reconvert it into a liquid, and these two operations constitute the process of distillation; the necessary apparatus, then, must consists of two parts, a boiler, or vaporizer, and a condenser, to which may be attached a separate receiving vessel. The condensed vapor is called the distillate.

The rationale of the process of distillation may be explained as follows: Heat is applied to a liquid in a closed vessel, and is absorbed, which causes the liquid to change its state of aggregation to that of vapor; the vapor enters the condensing tube, where it comes in contact with the cold surfaces chilled by water on the outside; immediately it begins to part with its latent heat, transferring it to the cold surface and the water, and assumes again its original liquid form.

The temperature of steam not under pressure is 100° C. (212° F.), in addition to which it carries a latent heat of 550° C. (990° F.); if steam is condensed and the distillate collected is to have a temperature of 50° C. (122° F.), at least 600° C. (1080° F.) of heat must be given off or transferred to the water in the cooler. In other words, each liter of water converted into steam requires 6 liters of water at 0° C. (32° F.) to convert it back into water having a temperature of 50° C. (122° F.).

Alcoholic vapor requires only about one-half as much cold water for condensation as aqueous vapor, since its sensible heat is 78.2° C. (172.7° F.) and its latent heat only 215° C. (387° F.). The sensible heat of the vapor of official diluted alcohol is 82° C. (179.6° F.), and its latent heat about 260° C. (468° F.).

As such large quantities of water for condensing purposes are not practically available, the same object is attained—the withdrawal of the latent heat from vaporized liquids as completely as possible—by a continuous supply of cold running water. It has been frequently observed in the preparation of distilled water that more rapid condensation takes place if the water surrounding the condenser be supplied slowly and thus allowed to become warm. The outlet, or lower end of the condensing tube, should always be kept coolest, hence cold water must be supplied at this point and carried upward. Care must also be observed that the application of heat and refrigeration be properly adjusted, so that vapor be not generated in excess of the capacity of the condenser.

The simplest form of distillatory apparatus consists of a flask, or retort, in which the liquid to be distilled is vaporized, and a receiver immersed in cold water, in which the vapor is condensed. When a flask is used, this is connected with the receiver by means of glass tubing, as shown in Fig. 167, while in the case of the retort connection is made either by means of an adapter, see Fig. 168, or by inserting the beak of the retort directly into the receiver, as shown in Fig. 169.

To cool the vapor still more thoroughly, the beak of the retort, or the tube connecting the flask with the receiver, may be wrapped in part with cotton cloth upon which a constant stream of cold water is allowed to trickle, the water being prevented from running into the receiver by suspending the end of the cloth in the receptacle for waste water. Tubulated retorts have almost entirely superseded the plain variety, as they possess the advantage of being more easily filled and cleaned, and also admit of the introduction of a thermometer or safety tube, through a cork in the tubulure. A safety tube (Fig. 170) is often

necessary in distillation from retorts or flasks, to allow the escape of large volumes of vapor accumulated and suddenly evolved, which otherwise might endanger the apparatus or cause the liquid to rise

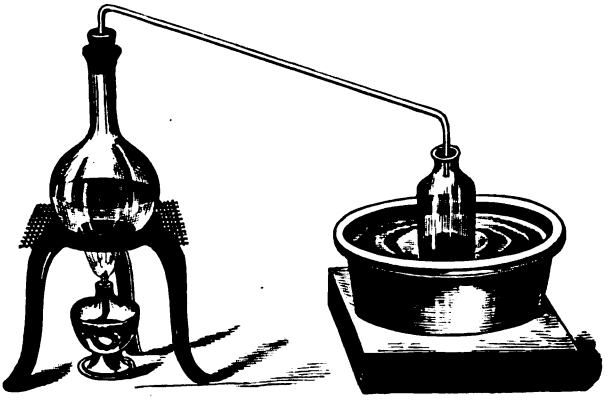


FIG. 167.—Simple distillation from a flask.

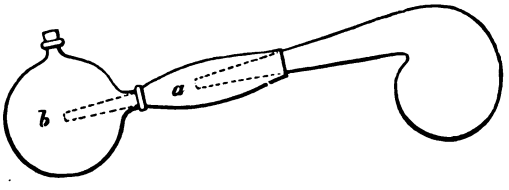


FIG. 168.—Plain retort with adapter, *a*, and receiver, *b*.

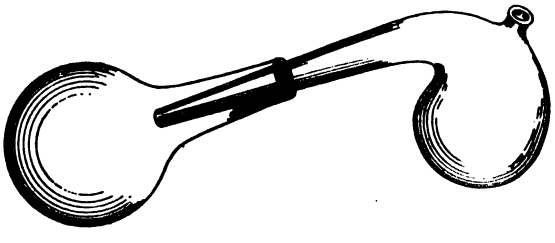


FIG. 169.—Tubulated retort and flask receiver.

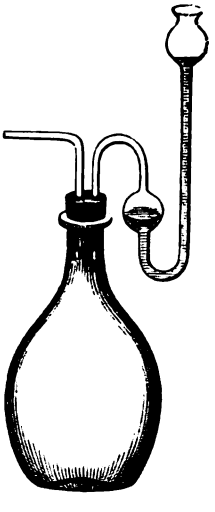


FIG. 170.—Safety tube.

and flow over into the condensing tube. Wide-mouth, flat-bottom flasks are preferable to retorts, as they can be more readily filled, connected and cleaned, and are easily supported on a sand- or water-bath.

For many purposes, when the most perfect refrigeration of vapor possible is desired, the apparatus known as the Liebig condenser will be found extremely useful, its construction being such as to insure a constant supply of cold water around the condensing tube, which

Fig. 171.—All-glass Liebig condenser, with adjustable clamp.

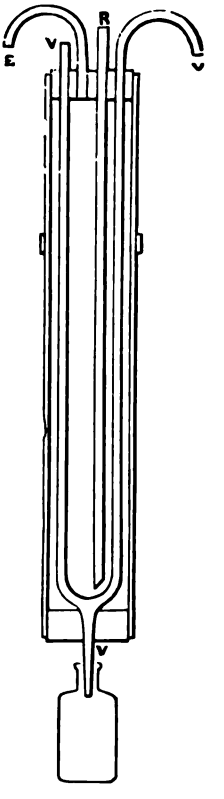


Fig. 172.—Squibb's upright condenser.

can be readily connected with any flask or retort by means of corks and glass tubing. The Liebig condenser consists of two tubes, one within the other; the inner always of glass, the outer of glass or metal and provided with attachments for supply and waste of water, which is made to enter near the lower end and to traverse the whole length of the outer tube before it is discharged at the upper end; therefore, as the vapor passes downward in the inner tube it is continually cooled and thus perfect condensation effected before it reaches the receiving vessel. Fig. 171 shows an all-glass Liebig condenser attachable to any

filtering stand and capable to being set at any angle or height, by means of the clamp support, to suit the position of the flask or retort with which it is to be connected.

In order to economize space on the laboratory table, the late Dr. Squibb devised an upright condenser, also made of glass, which can be attached, like the preceding one, to a stand; it is very effective, and differs from the Liebig condenser in having the condensing tube doubled like a U, shown in Fig. 172. The outer lines represent the water-case tube, *VV*, the vapor tube of U-shape with a small opening at the lower end, from which the condensed liquid escapes to a proper recipient, while any uncondensed vapor passes to the other leg of the tube, is there condensed, and flows downward to the outlet. *R* is the

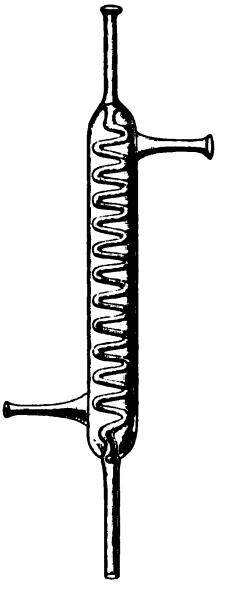


FIG. 173.—Reflux condenser.

FIG. 174.—Reflux condenser.

tube supplying cold water to the lower end of the water case, which rises and finally flows out through *E*.

Condensers intended for special purposes are often made of different designs, the same principle, however, being applied in all, namely, to bring the vapor in contact with a cold surface, kept so by a continuous supply of cold water. Thus the glass upright or reflux condensers shown in Figs. 173 and 174 are intended to be used in connection with a flask or an extraction apparatus for the purpose of condensing the vapor of alcohol, chloroform, ether, and similar liquids, and allowing the condensed fluid to flow back into the vessel from which the vapor issued. The spherical condenser, Fig. 175, is usually made of brass, and, occupying less space, is preferred by many to the upright

condensers; it is intended for the same purposes as the latter. A sectional view, shown in Fig. 176, explains the construction; the cold water enters at *a*, and filling the inner space is allowed to flow out at *b*,

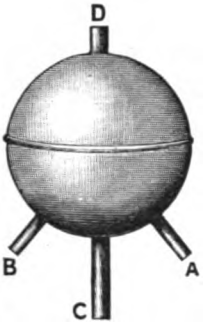


FIG. 175.—Spherical condenser.

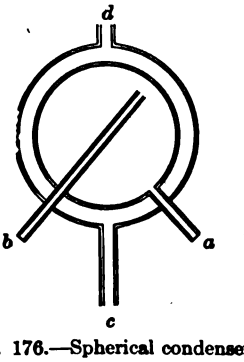


FIG. 176.—Spherical condenser.

while the vapor passes into the annular space surrounding the water reservoir, through the tube *c*, and having been condensed flows back again through *c;* the tube *d* is usually kept loosely corked, and is simply a safety attachment to allow the vapor to escape in case it should fail to be completely condensed.

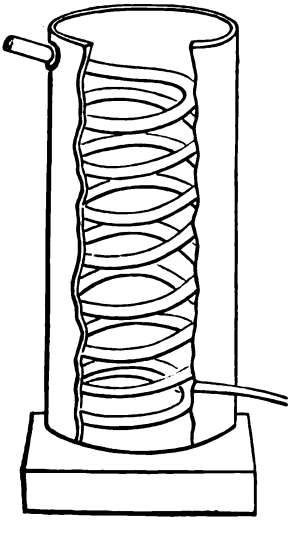


FIG. 177.—Worm condenser.

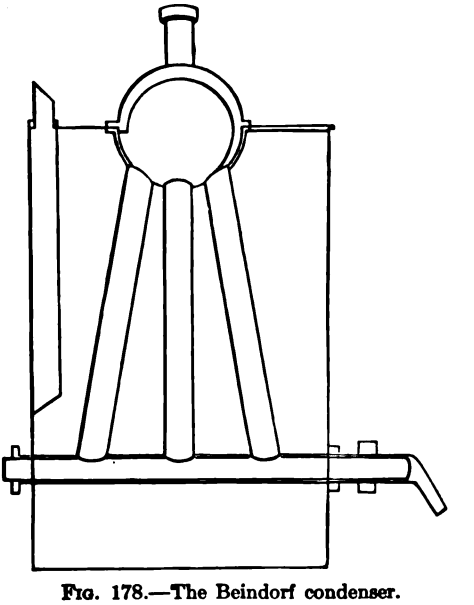


FIG. 178.—The Beindorf condenser.

For large operations, condensation of vapor is usually effected in a metal or stoneware tube bent in the form of a spiral, and known as a *condensing worm* (see Fig. 177), inclosed in a metal or wooden

case, which is kept supplied with a constant stream of cold water. On account of the difficulty encountered in cleansing the worm, other arrangements have been suggested, some of which are extensively employed in Europe. Fig. 178 represents the *Beindorf condenser*, in which the vapor is made to pass through three straight tubes, connecting with a common outlet tube; by unscrewing the upper half of the globular chamber into which the vapor first passes, all the tubes can be thoroughly cleansed. The *Mitscherlich condenser* (Fig. 179) differs from others in keeping the vapor in contact with two separately cooled surfaces, which insures more rapid condensation; as shown in the illustration, the condensing chamber consists of a somewhat tapering cylindrical vessel, *a*, ending in a tube, the whole made of metal (preferably block-tin), and resting on a support in a large metal or wooden case, *b;* into this condenser is accurately fitted at the shoulder a similar metal cylinder, *c*, cone-shaped at the closed end. By means of long funnel tubes cold water is continually supplied at the bottom of the outer and inner coolers, *b* and *c*, which rises as it becomes warmed, and flows out at the top at *d* and *b;* the distillate flows off into a receiver at *f*. In practice the Mitscherlich condenser has been found very effective, and if the inner cooler has been properly fitted to the condensing chamber, no escape of vapor need be feared; it is readily taken apart and cleaned, and the only apparent disadvantage lies in the double water supply and waste.

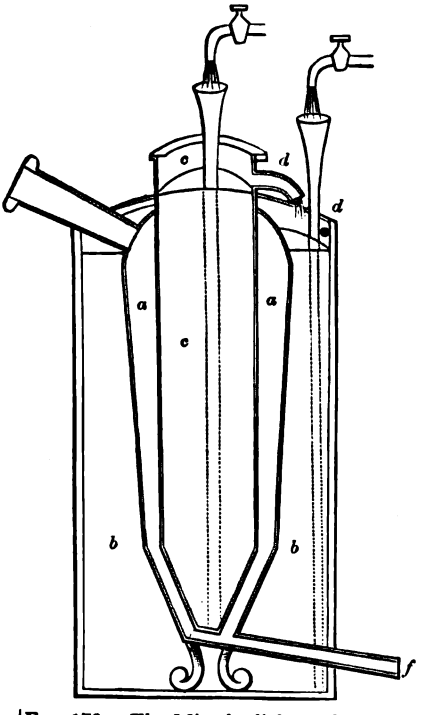


FIG. 179.—The Mitscherlich condenser.

It frequently happens, when distilling from glass flasks or retorts, that the liquid, although boiling at first quietly, suddenly begins to evolve vapor violently, the phenomenon repeating itself from time to time. This outburst of accumulated vapor is termed *bumping*, and although it has not been satisfactorily explained, it is known to occur chiefly in smooth glass vessels; it is both annoying and dangerous, as it may result in fracture of the vessel, or in the liquid splashing upward into the condensing tube. Bumping may be due to unequal heating of the vessel, for if the flask or retort be covered with a hood of pasteboard or metal, so that the heat be equally

diffused, it occurs but rarely, and less violently. Another remedy consists in introducing angular bodies into the liquid, such as pieces of pumice stone or glass, or a long platinum spiral, which will afford a ready means of escape for the vapor from the bottom of the liquid. Prof. Proctor, of England, has proposed as a very effectual remedy to pass a slow current of air, hydrogen, or carbon dioxide through the hot liquid; for small operations this may be done by forcing a stream of air, by means of an India rubber ball bellows, through a glass tube drawn out to a capillary tube and dipping to the bottom of the liquid, while heat is being applied. Ebullition is said to go on smoothly so long as this is continued, but bumping commences as soon as the supply of air ceases. Another plan which has been found very satisfactory, especially in the process of distillation, is the suction of air through the retort by means of an aspirator attached to the receiver.

For the recovery of alcohol from weak percolates in the concentration of vegetable solutions by distillation, special metallic stills have been devised. Those made of heavily tinned copper, of 1- to 5-gallon capacity, will be found most desirable for pharmacists. Figs. 180, 182, 183, and 185 represent different styles of pharmaceutical stills in use at the present time. Beck's pharmaceutical still (Fig. 180) is one of the best stills made for the concentration of weak percolates and the recovery of alcohol, and is especially adapted for the work of the small manufacturer. It is simple in construction, efficient in condensing power, and easily cleaned. It is made of heavily tinned copper, and the evaporating pan has a capacity of 2 gallons. The cold water, which is made to circulate freely between the double walls of the cone-shaped head, is supplied near the base on one side, at *a*, and discharged at the top on the other side, at *b*. The vapor is condensed on the under side of the still head, the distillate collecting in two gutters or troughs, one above the other, whence it is discharged through a common outlet, *c*, as shown in the sectional view. The waterbath and condenser are securely clamped together by means of six bolts and nuts, the rim of the evaporating pan being interposed between two flat rubber rings; an air-tight joint is thus produced and escape of vapor effectually guarded against. A small tube on the side of the waterbath is for the escape of steam, and if about 1½ gallons of water be put into the bath when the still is started, it will not require refilling for about twenty-four hours. If the quantity of liquid to be distilled is in excess of the capacity of the evaporating dish, the latter may be refilled by means of a long-stem funnel through the opening in the apex of the still head. The important features of the Beck still are: (1) A broad and rather shallow evaporating dish; since the liquid will be kept at a temperature below its boiling point, vaporization will take place wholly at the surface, and hence the larger the surface exposed the more rapidly will the vapor escape. (2) The two gutters or troughs on the under side of the still head, whereby the dripping back of any condensed liquid into the evaporating dish is

avoided, and thus the annoying feature of a single gutter arrangement overcome. (3) The capacity and style of the waterbath, which are

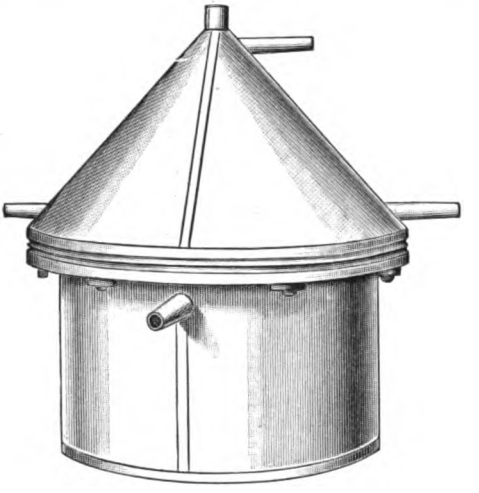


FIG. 180.—Beck's pharmaceutical still (exterior view).

such as to insure a supply of hot water or steam under and around the evaporating dish for many hours, since the escape of steam at the temperature employed is quite moderate. The Beck still can be heated

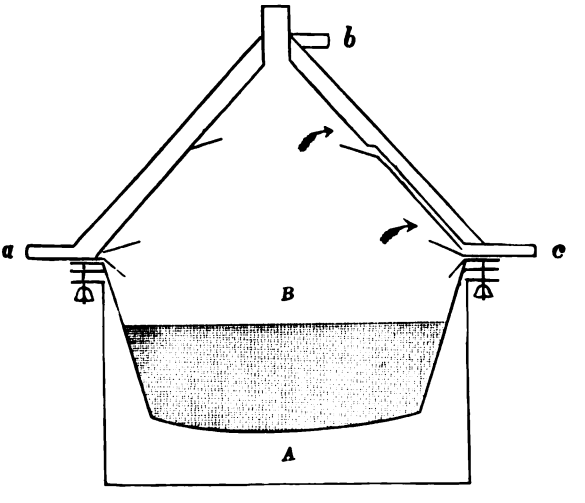


FIG. 181.—(Sectional view).

with either gas or oil, and if water attachments are not convenient, a barrel of cold water may be placed at some height above the still, from which the condenser can be supplied.

The special features of the Remington still (Fig. 182) are the peculiar shape of the still head and the construction of the condenser. In the former the opening for the passage of the vapor is drawn over to one side, instead of being in the center as usual, by which arrangement the condensing surface of the head is greatly reduced and condensation of vapor within the body of the still obviated as far as possible. The condensing tube represents a multiple Liebig condenser, 7 block tin tubes being so arranged within a copper case that cold water is constantly circulating between them. Two ground brass joints are used—one at the point of juncture of the condenser with the still head, the other where the nose piece is attached to the end of the condenser. The capacity of the still is 3 gallons, and by the

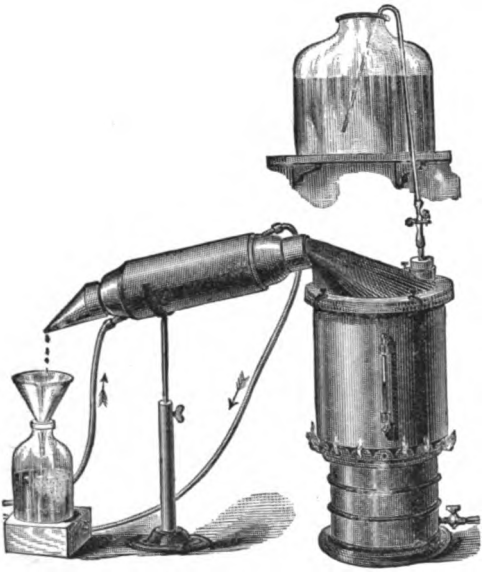


FIG. 182.—The Remington still.

siphon arrangement shown in Fig. 182 it is possible to feed the still from a reservoir while distillation is in progress.

The Prentiss alcohol reclaimer (Fig. 183) is easily operated. It is made of tinned copper, and is provided with an upright column, *B*, screwed to the top of the still, in which is placed a rod carrying a series of perforated tin disks (see Fig. 184) intended to increase the alcoholic strength of the distillate by condensing the aqueous vapor, which then returns to the still, while the vapor of alcohol passes on to the condenser proper. The vapor passes from the column through a short tube, *C*, to the condenser, which consists of a 12-ounce copper can, *D*, containing a tube bent zigzag, and supplied with cold water by means of a funnel tube, *E*, reaching to the bottom of the can.

The distillate is collected at the outlet, *G*, a continuation of the zigzag condensing tube, while the waste water flows out at *F*, which is connected with the sink by means of rubber tubing.

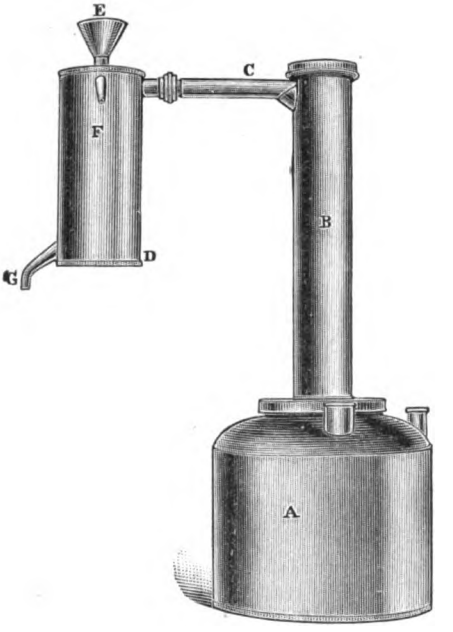


FIG. 183.—The Prentiss alcohol-reclaimer.

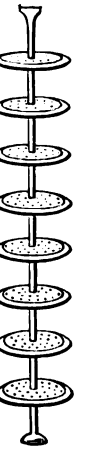


FIG. 184.

The Anderson automatic still (Fig. 185) differs from the others described in the continuous automatic supply of water to the water bath. The refrigeration of vapor is effected by a free circulation of water between the walls of the cone-shaped condenser, as in the Beck still, the distillate collecting in a gutter at the base of the cone. The water in the condenser gradually becomes warm and flows into the waterbath, which is kept filled to a uniform height by means of an overflow pipe, and thus the necessity of replenishing the boiler with cold water from time to time, in large operations, is obviated. The liquid to be distilled is heated in a broad, shallow evaporating dish, from which the alcoholic vapors rise rapidly owing to the large extent of surface exposed.

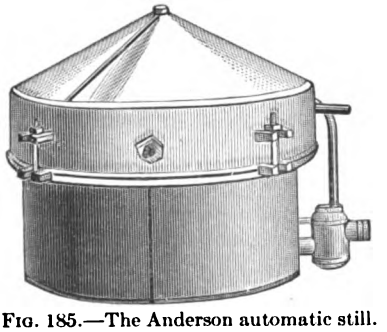


FIG. 185.—The Anderson automatic still.

Automatic stills are recommended and largely used for the dis-

tillation of water; but when absolute purity is desired it must not be overlooked that in automatic stills the air and other gases contained in the water are sure to pass out with the steam and redissolve in the condensed vapor, so that, while all non-volatile impurities are removed, volatile matter is liable to contaminate the distillate. Distilled water entirely free from air and all other impurities can be obtained only by rejecting the first portion of the distillate (about 10 per cent.), which contains the volatile matter, and allowing the last portion (about 10 per cent.) to remain in the still; this will retain all mineral impurities and such decomposition products as may result from the prolonged action of heat on organic constituents. Only about 80 per cent. of the volume of water to be distilled should be collected and considered absolutely pure. The tubes in which the aqueous vapor is condensed must be of glass or pure block tin.

In the manufacture of fluid and solid extracts and similar preparations, on a large scale, stills heated by steam are employed for the concentration of weak percolates and the recovery of alcohol. Such stills are made of heavily tinned copper, and will hold from 50 to 250 gallons of percolate. The boiler, or evaporating pan, is partly enclosed in a copper jacket provided with an inlet and outlet for steam, by which means heat is supplied to the liquid. Fig. 186 represents two of these steam stills. Condensation of the alcoholic vapor is effected by means of upright condensers, the latter usually consisting of a number of straight block tin pipes encased in a copper cylinder, on the principle of the Liebig condenser.

The still designed by Dr. Rice (see Fig. 187) presents the peculiarity of having the condenser situated immediately above the still head, which is for the double purpose of saving floor space and allowing the condenser to be used as a reflux condenser in the case of continuous percolation, as explained below. The case enclosing the condensing coil is made of copper, has a rounded bottom, and is closed at the top; cold water is supplied at the bottom at *B* by means of the rubber tube *A*, and is discharged at *C*, near the top, by means of a tube leading to the waste pipe *D*. The small tube near *B*, usually closed with a cork, is for the purpose of emptying the water without removing the tube *A*. The head of the still is provided with three short tubular openings, one for refilling the still when required, another for inserting a thermometer, and the third, shown in the cut, for carrying a safety tube, *L*. The vapor pipe starts from the still head at *E*, and is connected with the projecting end of the block tin condensing coil, near the upper part of the tank, at *E*. The worm inside of the condenser tank has a uniform downward descent, and emerges at *F*, extending a short distance to the joint, by means of which it is connected with a block tin pipe, *J*, leading to the receiving vessel. The head is attached to the body of the still by means of a rubber washer and iron clamps, and can be readily removed, after taking off the clamps, by attaching the tackle *K* to the top of the condenser and hoisting the whole upward.

Steam is admitted to the jacket at *N*, and *N* is the exhaust pipe for the same. About the middle of the lower projecting end of the condensing tube a branch passes downward back to the still at *G*, and terminates under the head in the form of an ω, which trap prevents any condensed liquid from flowing back into the still should the stopcock at *H* be open. The object of this branch pipe is to carry the condensed alcohol back to the still when the apparatus is used for

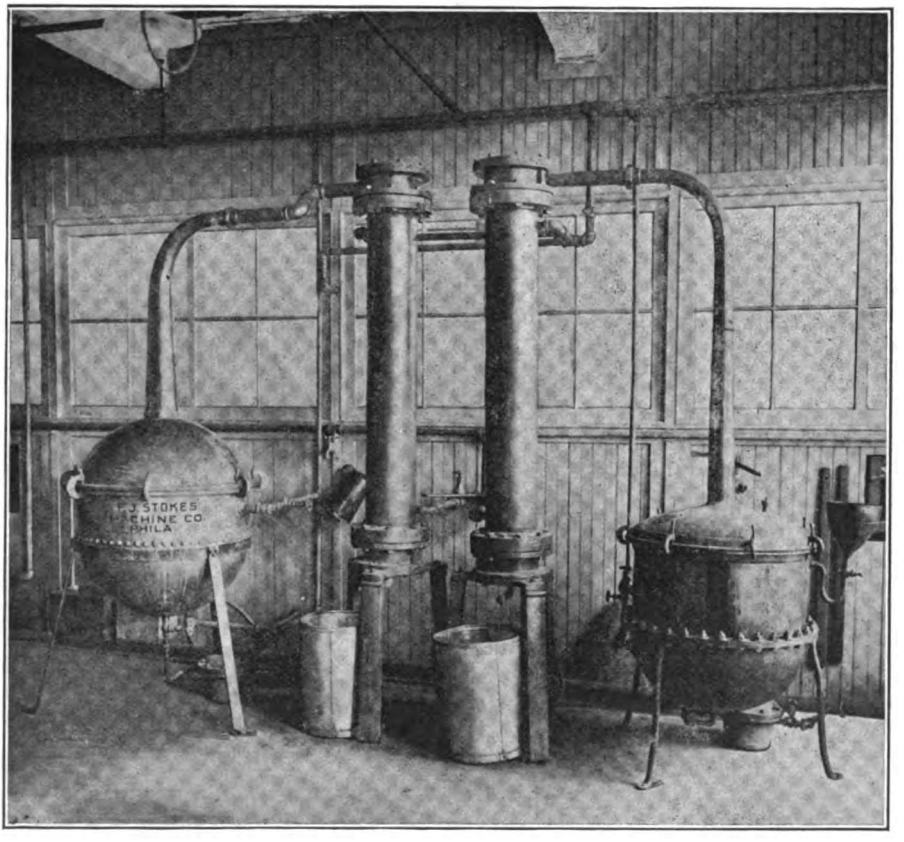


FIG. 186.—100-gallon copper stills, with upright condensers.

continuous percolation of such substances as nux vomica, aconite, etc. When the still is to be used for this purpose, a large tin-lined copper percolator, into which the moistened drug has been packed and covered with a felt diaphragm, is securely clamped between the head and the body of the still, into which menstruum has previously been poured. When steam is admitted to the jacket the alcohol is vaporized, recondensed above, and made to flow back to the still and on to the drug in the percolator by means of the branch pipe and stopcock at *H*, the

tube *J* having been disconnected and the joint closed with a cork. The percolate collects in the body of the still and the alcohol is again vaporized as before, the process continuing at the pleasure of the operator, and the drug being thoroughly exhausted with a minimum quantity of menstruum. Thus, prolonged digestion and continuous

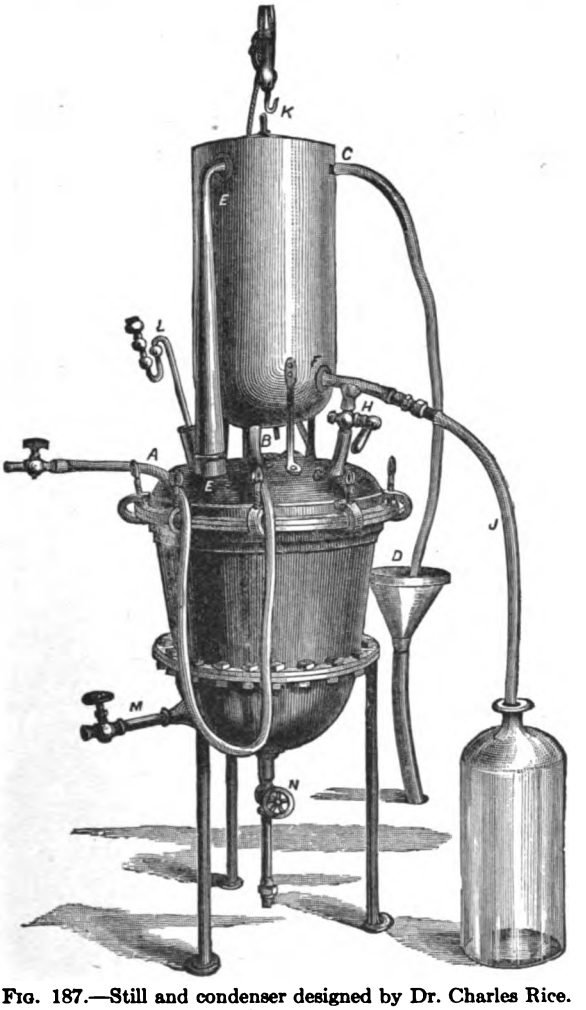


FIG. 187.—Still and condenser designed by Dr. Charles Rice.

percolation of large quantities of drugs can be successfully carried on in this apparatus without any loss of alcohol.

The so-called dreg stills for the recovery of alcohol from the exhausted drug left in the percolator (see Fig. 188), are much used by large manufacturing establishments. They have a capacity of from 25 to 300 gallons and are made of heavy galvanized iron or of copper, and

are provided with steam connections, from which a pipe leads into the body of the still to a perforated coil at the bottom, allowing the live steam to act directly on the dregs; a perforated diaphragm

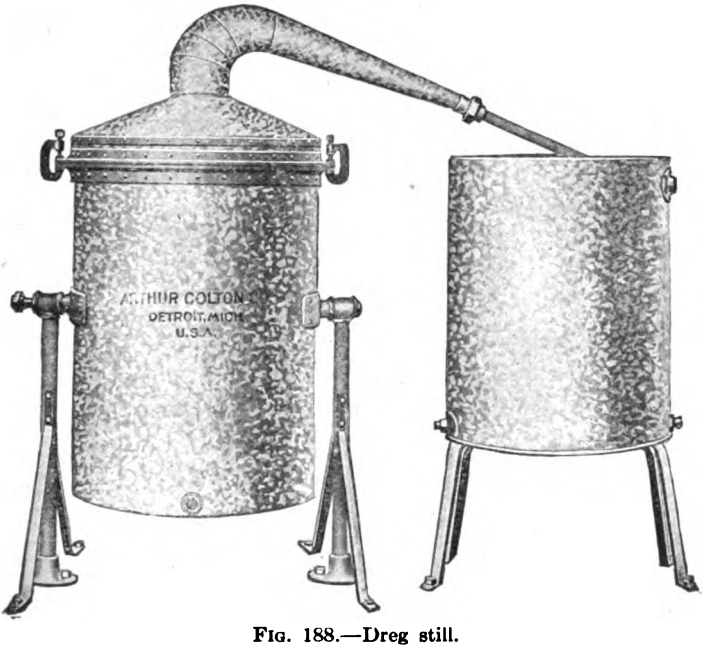


FIG. 188.—Dreg still.

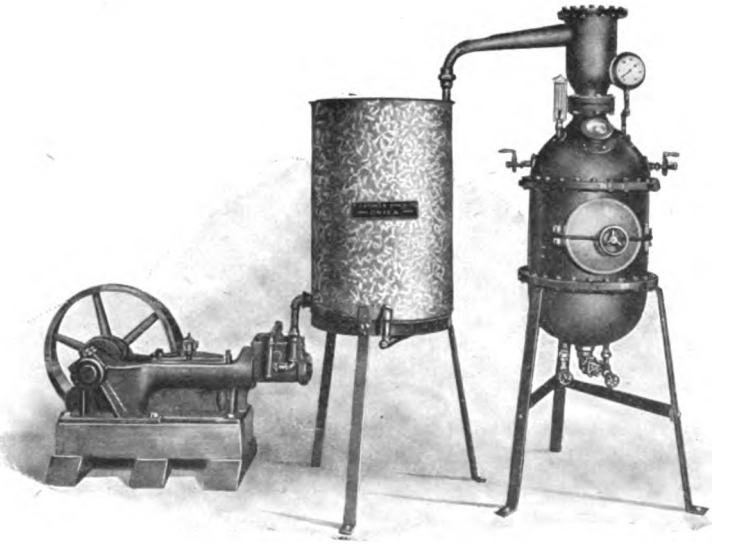


FIG. 189.—Vacuum still.

rests over the coil to prevent the dregs from packing too closely around it. The alcohol in the marc is rapidly vaporized and passes over into the worm condenser shown in the illustration.

Vacuum stills are necessarily of a somewhat different construction, and are used only in large manufacturing establishments, where the concentration of bulky vegetable solutions at low temperatures is frequently desired. Without the use of vacuum apparatus the concentration of alkaloidal and other percolates in the manufacture of

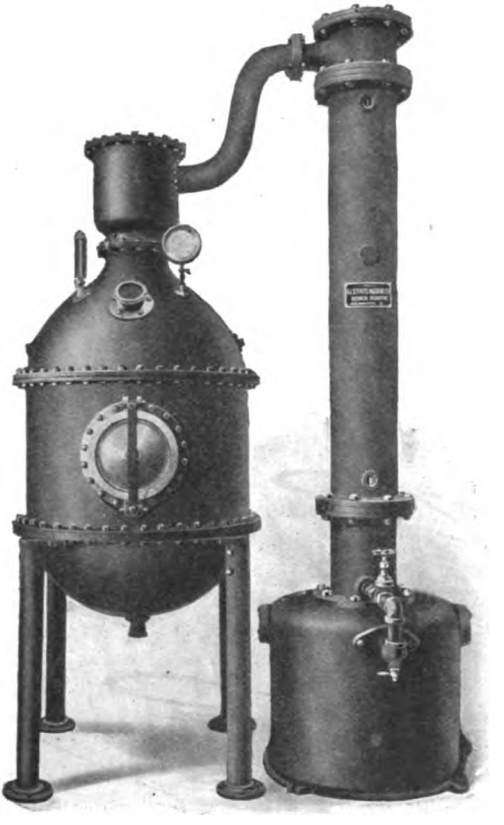


FIG. 190.—Large vacuum still.

fluid and solid extracts would frequently give rise to undesirable changes. Fig. 189 represents a modern vacuum still manufactured by the F. J. Stokes Machine Co., of Philadelphia, which is provided with a thermometer, vacuum gauge, sight glass for watching the operation, and a large man-hole for convenience in cleaning the still. The vacuum is produced by means of the pump shown in the lower left hand corner of the illustration, and frequently a suitable stirrer is provided within the still by means of which the liquid is kept in

constant motion while evaporation is going on. These stills are made of heavily tinned copper of various sizes, from 25 to 1000 gallons capacity, and are enclosed in a jacket to which steam is supplied. Fig. 190 represents one of the larger size vacuum stills provided with a vertical condenser mounted on a 50 gallon receiver for the distillate. The liquid to be concentrated in these vacuum stills is frequently supplied automatically to the still, so that the process of evaporation is continuous and large quantities of menstruum can be recovered in a comparatively short time. At the end of the operation the concentrated liquid is withdrawn from the bottom of the still by means of a faucet suitably attached.

Ebullition of the liquid in vacuum stills can readily be effected at a temperature of 49° C. (120.2° F.) and even lower, as shown in the following table, the temperature depending, of course, on the vacuum produced.

BOILING POINT OF WATER UNDER REDUCED PRESSURE.

Vacuum.	Temperature.
20 inches	72° C. (161.6° F.)
22 inches	67° C. (152.6° F.)
24 inches	68.5° C. (140.9° F.)
26 inches	52° C. (125.6° F.)
28 inches	38.5° C. (101.3° F.)
28.5 inches	33.5° C. (92.3° F.)
29 inches	26.3° C. (79.3° F.)

Fractional distillation is the name applied to a process intended to separate liquids of different boiling points, and is often a valuable aid in determining the composition of a mixture or in the purification of certain chemicals. It necessitates the introduction of an accurate thermometer into the retort, flask, or still, so that a change in the boiling point may be promptly observed and the receiving flask changed accordingly. As all liquids will begin to vaporize before their boiling point is reached, perfect separation, is impossible in a single operation; it is, therefore, customary to collect the liquids condensed during a certain range of temperature in the still, and to subject these again to the same process of fractionation, until finally a pure liquid showing a stationary boiling point is obtained. As an example, may be cited a mixture of ether, chloroform, and alcohol. If pure, the three liquids will boil at 35.5° C., 60.5° C., and 78° C., respectively; but a mixture may possibly boil at about 40° C., when almost all of the ether will distil over, together with small portions of chloroform and traces of alcohol. As the temperature rises to 65° C. the distillate will consist chiefly of chloroform mixed with traces of ether and small portions of alcohol; and finally, at 78° C., alcohol will distil over, not, however, entirely free from chloroform and traces of ether. By changing the receiving flask at 40° C., and 65° C., fractions will be obtained entirely different in composition from the original. If the first fraction be now distilled, the liquid

will probably boil near 38° C., and by carefully watching the thermometer and changing the receiver ether almost entirely free from chloroform and alcohol may be obtained. By thus carefully collecting the fractions at fixed temperatures, and re-distilling each by itself, more thorough separation is possible.

During the ebullition of a pure liquid no change of temperature will be indicated by the thermometer, but in a mixture of intersoluble liquids a gradual rise will continue as the more volatile are vaporized, this rise being slow or rapid as either the more volatile or less volatile liquids predominate. If a mixture of only partly miscible liquids be subjected to distillation, the temperature will remain stationary during the ebullition of the more volatile liquid and only begin to rise when the same has nearly all been vaporized. In such cases almost perfect separation can be effected, particularly if the boiling points of the liquids lie far apart. Examples: benzin and alcohol, or alcohol and oil of turpentine. Numerous coal-tar products are obtained by fractional distillation.

Fractional condensation is closely allied to fractional distillation, and is largely employed in the rectification of alcohol and the purification and concentration of glycerin and other liquids. It is effected by passing the mixed vapors into a series of condensers kept at regular temperatures, each succeeding one being cooler than the one which precedes it.

Destructive distillation is the process of heating dry vegetable or animal matter, in suitable closed vessels, until decomposition takes place, the volatile products being expelled and a fixed residue remaining. As the name indicates, the process involves the destruction of the original compound, whereby products of simpler composition are obtained. In order to avoid oxidation, destructive distillation must be carried on in closed apparatus with entire exclusion of air, and as the heat necessary is in most cases far greater than that to which glass vessels could be safely exposed, iron retorts or cylinders are employed. The residue left in the iron retort is often a fused mass insoluble in water, which necessitates mechanical means for its removal. The products of destructive distillation, in their crude state, are usually accompanied by a peculiar smoky odor called *empyreuma*, said to be due to an oil developed during the process of decomposition; this is subsequently removed by rectification. The most striking examples of destructive distillation are the manufacture of acetic acid from wood and of illuminating gas from coal.

SUBLIMATION.

Sublimation is the term applied to the process of vaporizing volatile solids and condensing the vapor back into a solid; it must not be confounded with the term *dry distillation*, which is frequently used in place of destructive distillation. The product of sublimation is

known as a sublimate, and may occur in the form either of a fine powder or compact masses.

The object of the process of sublimation may be the purification of a substance by separating the volatile solid from less volatile or fixed impurities, as in the case of sulphur, camphor, naphtalene, and iodine, or the separation and collection of volatile solids resulting from chemical reaction at higher temperatures, as in the case of pyrogallol, calomel, and mercuric chloride.

The apparatus consists of a subliming vessel made of iron, glass, or earthenware, and a condenser adapted to the volatility of the product, the condensing surface being kept sufficiently near the source of heat to avoid cooling of the vapor before it reaches the condenser. If the temperature of the condenser is but little below that of the subliming vessel, the vapors of the volatilized substance will not condense until they strike the surface of the condenser, and will form in compact masses, frequently in crystalline condition; as, for instance, arsenic trioxide, corrosive mercuric chloride, ammonium carbonate, and commercial sal ammoniac. In order to obtain the sublimate in the form of powder, the air in the condenser must be decidedly cooler than the temperature at which the substance volatilizes, because then the vapor will be immediately cooled and rapidly deposited in very small particles, as in the case of calomel, sulphur, and camphor when intended for subsequent compression.

The process of sublimation is confined to the larger operations of manufacturing chemists, but can be demonstrated in a small way by placing a few grains of camphor or iodine in a long test tube and then heating until all has been volatilized; in a few minutes the substance may be gathered in the form of very small crystals from the upper part of the tube.

CHAPTER XI.

CRYSTALLIZATION.

THE subject of crystallization, while a most important branch of mineralogy and chemical physics, is of less value in pharmacy proper; but as the Pharmacopœia makes frequent use of terms belonging to the study of crystallography, and as the pharmacist may have occasion to resort to crystallization for the purpose of determining the character and quality of substances, a short notice is deemed desirable.

Crystallization may be looked upon as another method of separation, as it is frequently employed for the purpose of removing impurities from crystallizable substances. The term *crystal* is applied to solid inanimate bodies of regular internal structure and definite geometrical form, bounded by plane surfaces and having angles of fixed and constant values. The assumption of such distinctive geometrical forms occurs, as a rule, during the change taking place in the state of aggregation of substances from the gaseous or liquid to the solid condition; in a few cases it occurs also in solid bodies, as iron and brass wire.

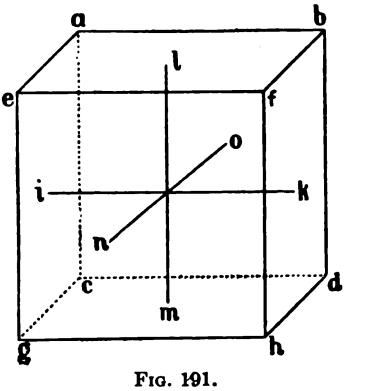


FIG. 191.

In the preliminary study of crystallography the meaning of the following terms must be considered.

Faces are the plane surfaces bounding the crystal (see *abdc*, *efhg*, *abfe*, and *bfhd*, Fig. 191).

Edges are the lines of intersection of two adjoining faces (see *ef*, *ab*, *fh*, *bf*, *db*, *eg*, *ea*, *gh*, *gf*, *cd*, *ca*, *cg*, etc., Fig. 191).

Angles are the points formed by intersection of three or more faces (see Fig. 191), *e*, formed by *abef*, *eacg*, and *efhg*; *f*, formed by *bdhf*, *baef*, and *efgh*; *c*, formed by *dhgc*, *adbc*, and *aegc*, etc.

Axes are imaginary lines drawn through the center of the crystal, around which the symmetrical deposit of matter has occurred during the formation of the crystal (see *ik*, *lm*, and *no*, Fig. 191).

Amorphous (without form) designates the absence of crystalline form and structure, as in acacia, starch, gelatin, etc.

Dimorphous or *trimorphous* (of *two* or *three* forms) indicates that the substance occurs in two or three distinct crystalline forms, as carbon, sulphur, etc.

Polymorphous means of many forms.

Isomorphous (of the same form) indicates that two or more substances to which the term is applied crystallize in the same form; thus the chlorides, iodides, and bromides of sodium and potassium are isomorphous. Isomorphous bodies are known to resemble each other also in chemical composition, and to permit of a ready interchange of constituents, as in the case of the various alums.

Cleavage is the tendency of most crystals to split in particular directions, affording usually even and frequently polished surfaces, the direction being always parallel with the planes of the axes, or with others diagonal to these. While some crystals cleave very easily, in others this tendency is scarcely discernible.

Tabular crystals are such as crystallize in flat plates, as potassium chlorate, iodine, strontium iodide, etc.

Laminar crystals are such as crystallize in thin plates, as acetanilid, betanaphthol, calcium hypophosphite, etc.

Acicular crystals are such as occur needle-shaped, as aloin, cinchonidine sulphate, quinin salts, etc.

Prismatic crystals are such as resemble a prism, being extended chiefly in the direction of the longest axis, as salicylic acid, santonin, cinchonine sulphate, etc.

Orthometric refers to the measurement of the angles, and is used to signify that the three axes intersect each other at right angles.

Clinometric refers to the intersection of the axes at oblique angles.

Holohedral, applied to crystalline forms, signifies that the full number of faces required by perfect symmetry are present.

Hemihedral signifies that only one-half the number of faces required by full symmetry are present.

Crystals are formed according to fixed laws of Nature, and there can be no doubt that the force of cohesion plays an important part in their formation; but no one knows how, nor why, the molecular particles of certain substances arrange themselves into symmetrical deposits, around a common center, in a manner to give rise to numerous distinct and definite forms.

The large variety of forms in which crystals appear depends entirely upon the number and length of the axes and their relative inclination—that is, the angles at which they intersect each other. All crystalline forms have been reduced by scientists to two main groups, the *orthometric* and the *clinometric* groups (see above), and these have again been subdivided into six systems: the orthometric group comprises the *regular*, *quadratic*, *rhombic*, and *hexagonal* systems: the clinometric group, the *monoclinic* and *triclinic* systems. As all crystals belong to one or the other of these systems, the salient features of each should be studied.

1. *The Regular System*, also known as the Monometric, Cubic, Octahedral, or Tessular System.

Crystals of this system have three axes of equal length, which intersect each other at right angles, as shown in Fig. 192.

The fundamental forms of this system are the cube and octahedron (Figs. 193 and 194).

Alum, phosphorus, arsenic, trioxide, diamonds, alkali iodides, chlorides, fluorides, and cyanides, as well as many metals and their sulphides, crystallize in this system.

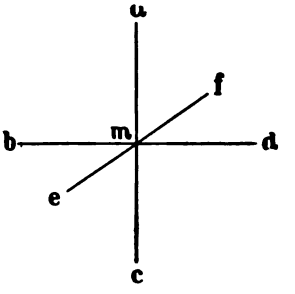


FIG. 192.—Axes of the regular system.

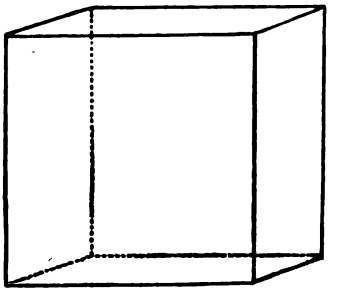


FIG. 193.—The cube.

2. *The Quadratic System,* also known as the Dimetric, Square Prismatic, or Tetragonal System.

Crystals of this system have three axes intersecting each other at right angles, two of which are of equal length and one either longer or shorter than the other two; the two equal axes are called secondary axes, while the third is termed the primary axis (see Fig. 195.)

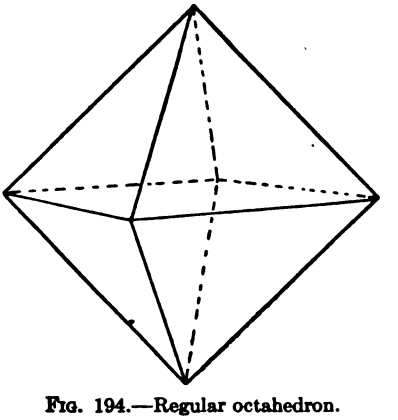


FIG. 194.—Regular octahedron.

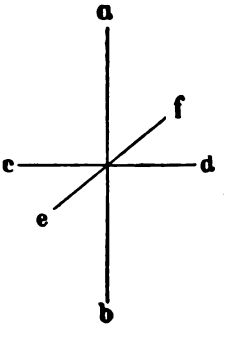


FIG. 195.—Axes of the quadratic system.

The fundamental forms of this system are the quadratic octahedron (also called square-based double pyramid) and the right-square prism (Figs. 196 and 197). The pyramids of this system have square bases.

Among the modified forms are the truncated quadratic octahedron (Fig. 198) and the quadratic pyramidal prism (Fig. 199).

Potassium ferrocyanide, calomel, nickel sulphate, boron, tin, stannic oxide, magnesium sulphate, zinc sulphate, etc., crystallize in this system.

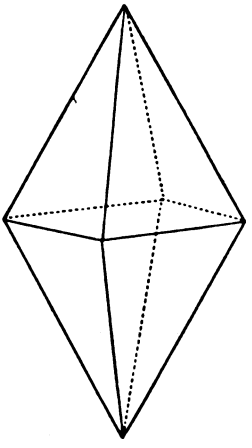


FIG. 196.—Quadratic octahedron.

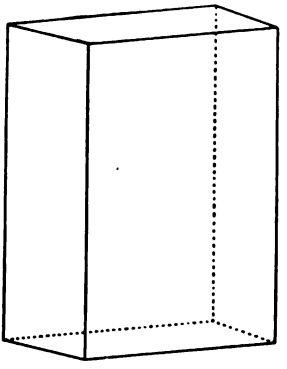


FIG. 197.—Right-square or quadratic prism.

3. *The Rhombic System*, also known as the Trimetric or Right Prismatic System.

Crystals of this system have three unequal axes intersecting each other at right angles, shown in Fig. 200. The fundamental form of this system is the rhombic octahedron or right rhombic double

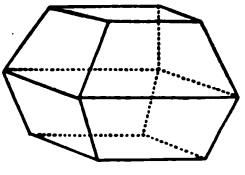


FIG. 198.—Truncated quadratic octahedron.

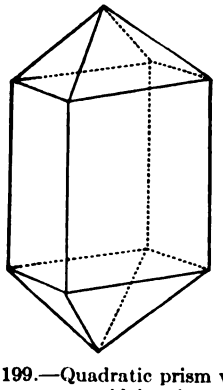


FIG. 199.—Quadratic prism with pyramidal ends.

pyramid (see Fig. 201). A modified form is the rhombic six-sided prismatic pyramid (Fig. 202).

Potassium sulphate and nitrate, resorcin, zinc sulphate, citric acid, iodine, Rochelle salt, mercuric chloride, barium chloride, tartar

emetic, codeine, salicylic acid, piperin, Epsom salt, silver nitrate, ammonium sulphate, cream of tartar, etc., crystallize in this system.

4. *The Hexagonal or Rhombohedral System.* Crystals of this system have four axes three of which are of equal length and are

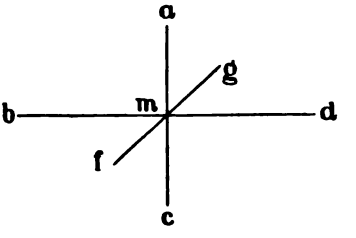


FIG. 200.—Axes of the rhombic system.

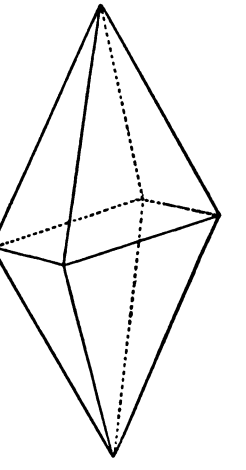


FIG. 201.—Rhombic octahedron.

called secondary axes, while the fourth, known as the primary axis, is either longer or shorter than the other three. The primary axis is at right angles to the plane of the secondary axes, which intersect each other at acute angles (see Fig. 203).

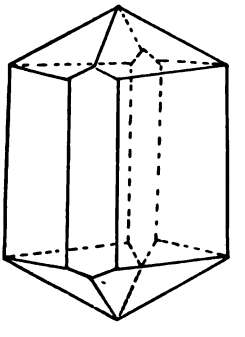


FIG. 202.—Rhombic prism.

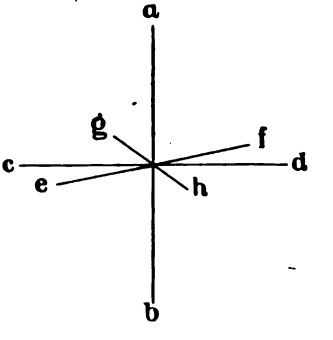


FIG. 203.—Axes of the hexagonal system.

The fundamental form is the double six-sided pyramid (Fig. 204). The rhombohedron (Fig. 205) and the regular six-sided prism (Fig. 206) are modifications of this system.

Sodium nitrate, camphor, graphite, ammonium chloride, ice,

calcspar, thymol, metallic bismuth and antimony, arsenic, silicic acid, etc., crystallize in this system.

5. The *Monoclinic System*, also known as the Monosymmetric, Clinorhombic, or Oblique Prismatic System.

Crystals of this system have three unequal axes, two being obliquely inclined to each other, the other axis forming right angles with these two (see Fig. 207).

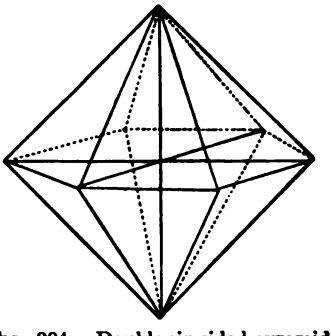


FIG. 204.—Double six-sided pyramid.

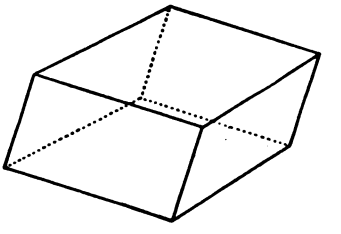


FIG. 205.—Rhombohedron.

The fundamental forms of this system are the monoclinic double pyramid or octahedron (Fig. 208), and the monoclinic prism (Fig. 209).

Ferrous sulphate, borax, lead acetate, cupric acetate, tartaric acid, potassium chlorate, and sodium acetate, sulphate, thiosulphate, phosphate, and carbonate crystallize in this system.

6. The *Triclinic System*, also known as the Asymmetric, Clinorhombohedral, or Doubly Oblique Prismatic System.

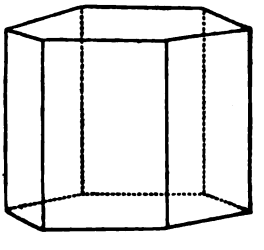


FIG. 206.—Six-sided prism.

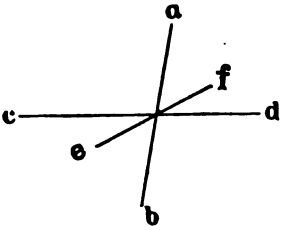


FIG. 207.—Axes of the monoclinic system.

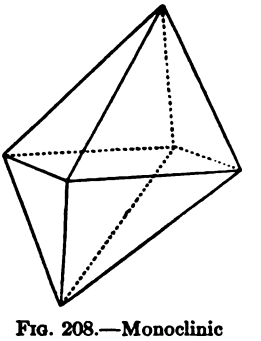


FIG. 208.—Monoclinic double pyramid.

This is the least regular of all the systems, the crystals having unequal axes, all obliquely inclined to one another (see Fig. 210).

The fundamental forms of this system are the triclinic prism (Fig. 211) and the triclinic octahedron or double pyramid (Fig. 212).

Cupric sulphate, potassium dichromate, gypsum, boric acid, manganous sulphate, etc., crystallize in this system.

The pyramidal form of crystals is found in all the systems above described, while the cube is confined to the regular system, and prisms are met in all but the regular system. The proper classification of a crystal may be determined by measurement of the angles and subsequent calculation of the length and inclination of the axes; the instrument used for this purpose is known as a goniometer.

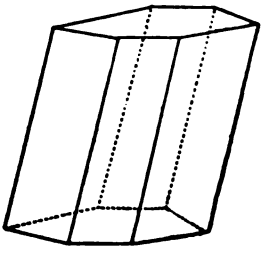


FIG. 209.—Monoclinic prism.

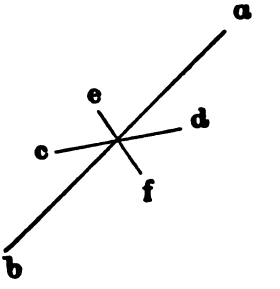


FIG. 210.—Axes of the triclinic system.

Various methods are employed for obtaining crystals, dependent upon the nature of the substance to be crystallized: thus, by sublimation; by deposition from supersaturated solutions as they cool; by deposition from solutions during slow evaporation of the solvent; by precipitation; by fusion and partial cooling; by the action of a galvanic current upon a solution; and by the addition of a substance having a strong affinity for the solvent, thereby withdrawing it from

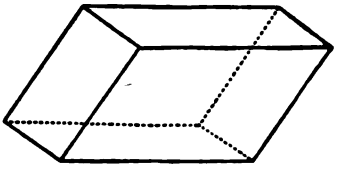


FIG. 211.—Triclinic prism.

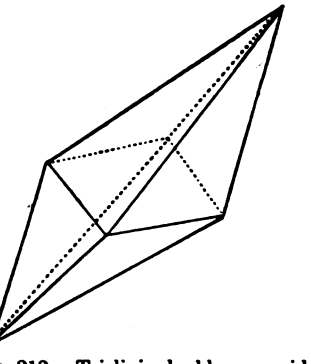


FIG. 212.—Triclinic double pyramid.

the solution. The method generally followed is the gradual separation from supersaturated solutions as they cool; if a solution of saline matter made with aid of heat is allowed to cool slowly, the water will gradually evaporate, and in some cases a part of it will unite intimately with the soluble substance to form crystals. Water which is thus appropriated, and which is essential to the constitution of the crystals, is

called *water of crystallization;* it varies greatly for different substances, ranging from 5 to 60 per cent. of the weight of the crystals. Crystalline bodies in which this water is entirely absent are said to be anhydrous. Some salts combine with various proportions of water of crystallization according to the temperature at which crystallization takes place, the crystals assuming different forms according to the amount of water taken up; sodium carbonate, sodium phosphate, and zinc sulphate are examples of this class.

Some crystals will part with a portion of their water of crystallization when exposed to the air, particularly if the latter is slightly warm; they gradually lose their transparency and the surface becomes opaque from the separation of dry powder. This change is termed *efflorescence*, and is frequently observed in Epsom salt, sodium carbonate, and borax. Other crystals are inclined to absorb moisture from the atmosphere, and in some instances to such an extent as even to liquefy; the terms *hygroscopicity* and *deliquescence* are used to designate this peculiar property, the latter applying to the more aggravated form. Potassium hypophosphite, zinc chloride and iodide, potassium acetate and carbonate, and lithium bromide are examples of deliquescent crystals. As a rule, crystals containing water of crystallization do not absorb moisture from the air, although calcium chloride, potassium citrate, and sodium hypophosphite are marked exceptions.

Besides the water needed for crystallization, some is also at times mechanically retained within the crystal during the formation of the latter, and is violently expelled upon application of heat; such water is called *interstitial water*, because it fills small interstices or spaces in the crystal, and *water of decrepitation*, because it causes the crystals to decrepitate or crackle when heated, due to slight explosions caused by the escape of aqueous vapor from a confined space. It is impossible to crystallize by a single operation all of the substance held in solution —a portion will remain in solution in some of the water, and this liquid constitutes the *mother-liquor*, which also retains the more soluble impurities. By further concentration the mother-liquor may be made to yield additional crops of crystals.

The time necessary to complete crystallization will vary with the nature of the dissolved body; the end may be assumed to have been reached when the solution has attained the temperature of the surrounding atmosphere, and the time for this must vary, since the dissolved body, by again taking on the solid form, is continually giving out latent heat to the surrounding solution, and thus the actual cooling is retarded. For small quantities and not very soluble substances twenty-four to thirty-six hours should be allowed, while large volumes of solution of readily soluble matter will require from three to six or eight days.

In order to obtain large and well-formed crystals the solution should not be made too concentrated, and should be carefully filtered to obtain a perfectly clear liquid, which should be allowed to remain

undisturbed and protected against dust, in a moderate temperature; it is the very slow evaporation of the solvent that enables the particles of dissolved matter to arrange themselves harmoniously and symmetrically around the center of the crystal forming. Perfect rest is equally essential, as agitation of the crystallizing solution tends to disturb the gradual uniform deposit and causes the formation of small and imperfect crystals, as in the case of commercial magnesium sulphate, zinc sulphate, etc.

The proper degree of concentration of the solution must be determined by the solubility of the substance to be crystallized. If the substance is only moderately soluble, the solution may be evaporated until a crystalline crust or pellicle begins to form on the top of the liquid; but in the case of very soluble substances such a degree of concentration would be too great, and a better plan is to evaporate the solution until a small portion transferred to a glass plate crystallizes within a reasonable length of time. In large operations the manufacturer relies upon the density of the solution as indicated by the hydrometer, and evaporation is continued to such a point as experience has taught to be most desirable for perfect crystallization.

The vessels best adapted for crystallization are deep rough-glazed stoneware basins, called crystallizers, frequently arranged with a lip to facilitate decantation of the mother-liquor; wooden vats are also extensively employed by manufacturing chemists, and in some cases these are lined with lead. For very small opertions glass or porcelain dishes may be employed, but their smooth surface is not favorable to the deposit of crystals.

Crystallization is often facilitated by placing insoluble foreign substances in the solution, which form starting-points or nuclei for the process, and to which the crystallizing substance readily attaches itself; pieces of string, wire, wood, etc., may be used for the purpose. Sugar is thus crystallized in the form of rock-candy, by stretching strings transversely across the boxes and tubs into which the syrup is poured.

Since crystals do not increase in size from within, as do animals and plants, but grow from without, by deposition of solid matter upon their surface, it is possible to procure large and well-formed crystals, for specimen purposes, by suspending a crystal in a saturated solution of its own constituent matter. This proceeding may be termed *nursing* a crystal. Isomorphous crystals are capable of growing in each other's solution; hence if a crystal of potassium alum be suspended in a solution of ferric alum or chrome alum, the latter will be found uniformly deposited, and thus a complete envelope of chrome or ferric alum will grow on the original crystal of potassium alum.

CHAPTER XII.

CLASSIFICATION OF THE NATURAL PRODUCTS USED IN PHARMACY.

PLANTS, either spontaneously or after subjection to various processes, yield certain vegetable substances which are extensively employed in pharmacy, and which, owing to their different characteristics as to composition, solubility, etc., have been divided into distinct classes, thus: gums, resins, oleoresins, gum-resins, balsams, fats, volatile oils, etc. Unfortunately the names which from long usage have been applied to some drugs are not in all cases indicative of their nature; hence a knowledge of the characteristic properties of each class of plant products is essential to guard against errors in nomenclature, which are of daily occurrence in commercial transactions; for instance, the names *balsam of fir* and *balsam copaiba* are applied to substances belonging to the class of oleoresins, and not containing any of the principles which characterize the balsams; *gum guaiac* and *gum mastiche* are true resins; *gum benzoin* belongs to the class of balsams; and *gum opium* is an inspissated juice of complex composition. None of the four last-named substances possesses any of the properties of the gums.

True Gums.—True gums are amorphous exudations wholly soluble in cold water, which are not affected by iodine, but are precipitated by alcohol and solution of lead subacetate, the latter being a most delicate reagent for the presence of gums. Neutral or normal lead acetate is readily miscible with solutions of the true gums, of which acacia may be taken as a type. A class of substances formerly called gums are now more appropriately known as *mucilages*, because they differ in several respects from true gums; they are not completely soluble in water (cold or hot), but absorb the same, and in some instances swell to a gelatinoid mass. Mucilages are frequently mixed with starch, which is easily detected by the blue color produced upon addition of iodine solution. Tragacanth and the gummy constituents of flaxseed, elm bark, quince seed, etc., belong to the class of mucilages.

Resins.—Resins are secretory products, in some instances the result of oxidation of volatile oils, and are widely diffused in the vegetable kingdom; they are wholly insoluble in water, except in the presence of caustic alkalies, but are readily soluble in alcohol, ether, and chloroform, and frequently in fixed and volatile oils. Resins are mostly solid and brittle at ordinary temperatures, generally amorphous, readily fusible and inflammable, become negatively electric by friction, decompose before volatilizing, and are precipitated from their solutions

by water and acids. Pine resin, mastiche, jalap resin, and guaiac resin are examples of this valuable class of plant products.

Oleoresins.—Oleoresins occupy a position intermediate between resins proper and volatile oils, and partake of the properties of both classes; their existence confirms the view held as to the formation of some resins in plants, and their consistence varies with the relative proportions of resin and volatile oil. Like the resins proper, oleoresins are insoluble in water, but soluble in alcohol and ether; they possess a marked odor, due to the volatile oil present, which latter can be separated by distillation, leaving the resin as a solid residue. White turpentine is an example of solid oleoresins, and copaiba of liquid oleoresins.

Gumresins.—Gumresins exist in plants in the form of an adhesive milky juice composed of variable mixtures of resin and gum suspended in water; they are obtained as exudations, by wounding the stem or root of the plant and allowing the juice to dry spontaneously. The proportion of gum and resin varies considerably, not only for different gumresins, but also for different samples of the same gumresin, and those lots are most valuable which contain the largest amount of resin. The activity of the drug resides wholly in the resin, and this fact is taken into consideration in the official formulas for the tinctures of asafetida and myrrh. A characteristic of gumresins is that when properly triturated with water they yield milk-like mixtures, termed emulsions, which fact is due to the suspension of very finely divided resin in the solution of gum; these milk-like mixtures cannot be obtained if the commercial finely powdered gumresins be triturated with water, but require the use of the natural product in coarse powder. As prominent gumresins, may be mentioned asafetida, myrrh, scammony, and ammoniac.

Balsams.—Balsams are either resinous or oleoresinous secretions containing benzoic or cinnamic acid, or both; it is the presence of these acids which distinguishes the balsams from ordinary resins and oleoresins. Balsams are soluble in alcohol, ether, and chloroform, but insoluble in water, although the balsamic principles can be extracted by sublimation or by treatment with hot water. Benzoin and balsam of tolu are examples of resinous balsams, while storax and balsam of Peru belong to the oleoresinous variety.

Fats.—The fats used in pharmacy are derived mainly from the vegetable kindgom, although a few animal products belonging to the same class are also employed. When liquid at ordinary temperature they are usually designated as fixed oils, although this name is also applied to one vegetable fat, solid and even brittle at 15° C. (59° F.); when strictly pure they are, as a rule, colorless, odorless, and tasteless. Fats proper are of a soft consistence and mostly yield liquid fats when subjected to a gradually increased pressure; those of a firmer consistence are usually termed tallows or suets, and such as are brittle at common temperatures are known as waxes, but these latter are not true fats. The origin of fixed oils in plants is supposed to be the starch,

while in animals fats are derived from the carbohydrates and fats consumed. Fats are lighter than water, and insoluble in that liquid; sparingly soluble in cold alcohol, with one or two exceptions; but, as a rule, freely soluble in ether, chloroform, petroleum benzin, carbon disulphide, benzene, etc.; a hot alcoholic solution of fats, in most instances, will deposit them in a crystalline condition upon cooling. All fats, whether liquid or solid, are greasy to the touch, and when dropped upon paper produce a stain which cannot be dissipated by heat; they have boiling points varying from 260° to 300° C. (500° to 572° F.), and frequently, when thus heated, undergo decomposition and give off acrid, irritating vapors. Fixed oils usually have a specific gravity of from 0.900 to 0.930 at 15° C. (59° F.), though occasionally as high as 0.970, as in the case of castor oil; many oils do not congeal until the temperature has fallen considerably below 0° C. (32° F.), while others deposit solid matter at 10° C. (50° F.). Like water, fixed oils expand upon congealing, and have been known to burst the vessels containing them. Fats are not inflammable, but will burn more or less readily with the aid of a wick. Nearly all vegetable and animal fats consist of a mixture of two or more fats, and when exposed to the air become oxidized, many of them gradually acquiring a disagreeable odor, due to the liberation of odorous fatty acids; this condition is known as *rancidity*, and may be avoided by keeping the fats as free from moisture as possible, in air-tight containers stored in a dry, cool, and dark place. Rancid fats may be improved, and to a certain extent restored, by washing them with warm water, or by treating them with magnesia or other weak alkali, and afterward washing them well. During the oxidation of fats by exposure to air heat is always developed, and certain fabrics, such as woollen and cotton rags, which are known to be poor conductors of heat, are liable to spontaneous ignition if saturated with fats and exposed to the air for some time. Fixed oils may be conveniently divided into *drying* and *non-drying* oils; the former upon exposure to air gradually thicken, and if in thin layers form varnish-like masses, whereas the non-drying oils remain fluid and become rancid.

Although fats are found in various parts of plants, those intended for use are collected exclusively from the fruit and seed, and are obtained either by expression or by extraction with some suitable solvent; the former process yields somewhat lower results, but is preferred because less troublesome and productive in many cases of a superior article. In Fig. 213 is shown an hydraulic press extensively used for the expression of mustard, cottonseed, and linseed oils. The crushed material, after being heated somewhat, is placed in sacks or press-cloths between the series of plates, and pressure applied from below, the oil being collected in the large box or trough, and from there delivered into the receiving vessel. The residue from certain seed expressions is used, under the name of *oil-cake*, as food for cattle and hogs and for fertilizing purposes. Cold expression yields

a finer oil than when heat is employed, although slight warming is generally resorted to so as to render the oil more fluid in the seed and thus insure a better flow. Expressed oils are always more or less contaminated with impurities, such as mucilaginous and albuminous matters, which are removed by allowing the oil to settle in large tanks and drawing off the clear liquid. Frequently filtration is employed for improving the quality of the oil, felt or flannel bags being best adapted for this purpose. When purification of fixed oils becomes necessary, they are treated either with sulphuric acid, caustic alkalies, zinc chloride, tannin, or alkali carbonates, and subsequently washed with hot water, after which they are carefully decanted.

The extraction of fixed oils is conducted in specially constructed extractors, frequently so arranged that the solvent is made to act upon successive portions of crushed seed, the saturated solution of fat being then transferred to a suitable distilling apparatus, where the solvent is recovered, to be used again for subsequent operations. The solvents usually employed are petroleum benzin of low boiling point and carbon disulphide; the oil is obtained in larger quantity than by expression, and is free from many impurities often found in expressed oils.

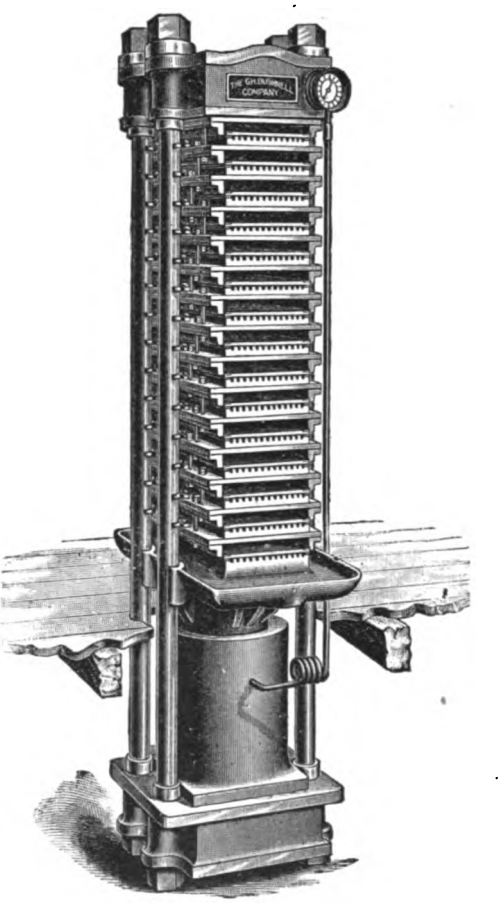


FIG. 213.—Steam press for fixed oils.

Fixed oils are frequently subjected to a bleaching process, which consists in treating the oil with solution of hydrogen dioxide, potassium permanganate, potassium dichromate, chlorine, or sulphurous acid; of these methods, the hydrogen dioxide process is preferable, as it is least liable to injure the oil, while the use of other bleaching agents necessitates repeated washing of the oil with water and even weak alkali solutions to remove acid oxidation products.

The adulteration of fixed oils is effected by mixing the finer and more valuable oils with inferior and cheaper varieties, and as the crude methods of former years are no longer practised, a better knowledge of the chemical behavior of fats and fixed oils is necessary at the present day. Caustic and carbonated alkalies are practically without effect upon fats and fixed oils in the cold unless free acids, due to rancidity, be present; a more or less uniform mixture results, but no chemical change is produced. If boiled together with solutions of alkali hydroxide or carbonate, all fats and fixed oils used in pharmacy with the exception of lanolin, wax, and spermaceti, readily undergo saponification and form water-soluble compounds known as soaps, glycerin being liberated at the same time.

Drying oils may be distinguished from non-drying oils by their behavior with sulphuric and nitrous acids. If 50 Gms. of a fixed oil be mixed with 10 mils. (or Cc.) of concentrated sulphuric acid, heat will be developed varying in intensity for different oils, the drying oils always showing the greatest rise in temperature; thus, while olive oil increases 42° C. in temperature, castor oil 47° C., and oil of almond 52° C., hempseed oil will show a rise of 98° C. and linseed oil 103° C. When mixed with nitrous acid, non-drying oils will gradually be converted into a solid mass, while drying oils remain fluid even after prolonged contact, although a few become somewhat thicker. The test is made by agitating for a short time 1 part of copper foil with 5 parts each of nitric acid and the oil, and setting the mixture aside for about six hours, when solidification is generally completed. Among the prominent non-drying oils are olive oil, castor oil, almond oil, lard oil, sesame or benne oil, croton oil, colza or rapeseed oil, and peanut oil; while the following belong to the drying oils: linseed oil, cottonseed oil, poppyseed oil, hempseed oil, and walnut oil.

Animal fats are usually obtained by rendering over a slow fire and then straining to remove the particles of membranous tissue.

The chief use of fats in pharmacy is in the preparation of liniments and ointments, and for this purpose they should be absolutely free from rancidity, and should be preserved in tightly closed, impervious containers in a cool, dry place.

Of the fats recognized in the Pharmacopœia 6 are of animal origin—lard, cod liver oil, suet, wool fat, spermaceti, and wax; and 8 are of vegetable origin—castor oil, cottonseed oil, croton oil, expressed oil of almond, linseed oil, olive oil, sesame oil, and oil of theobroma.

Lard (Adeps, U. S. P.).—This is the prepared abdominal fat of the hog derived from the so-called leaves, and preferably collected in the winter or early spring, as it has a higher fusing point than that collected in summer. For pharmaceutical purposes lard entirely free from water should be used; such lard, commercially known as *dehydrated lard*, is prepared by melting leaf-lard with just sufficient waterbath heat and then adding some substance having great affinity for water, but not affecting the lard itself, such as dried calcium

sulphate or anhydrous calcium chloride, sodium sulphate, or magnesium chloride. After keeping the melted lard in contact with the dehydrating agent for an hour or more, with frequent stirring, it is carefully strained and then stirred until cool. If much water is present in the lard, a dense liquid layer is likely to be formed in the bottom of the dish if either of the three last-named salts be used, from which the lard can be readily poured off. Dehydrated lard is now manufactured on a large scale, and may be purchased from the leading wholesale druggists at prices but little above the market price of ordinary lard.

Pure lard is liable to become rancid if kept for some time, hence the Pharmacopœia directs its preservation by benzoinating. This is done by thoroughly mixing 10 parts of coarsely powdered Siam benzoin with 1000 parts of lard, melting the mixture in a covered vessel on a waterbath, and, while frequently stirring, keeping up the temperature, not to exceed 60° C. (140° F.), for two hours; the mixture is then strained and allowed to cool. As lard contains liquid as well as solid fats, having different congealing points, it is necessary to stir the strained mixture until it assumes a creamy consistence, in order to avoid a granular condition. The balsamic principles of benzoin are soluble in the melted fat, and protect it afterward against change. In summer benzoinated lard, which is officially known as *Adeps Benzoinatus*, should contain 5 per cent. of white wax, in place of a like quantity of lard, to render it firmer.

Ordinary commercial lard has been found to contain water, starch, alkalies, and table salt, and occasionally an admixture of other animal fats and of cottonseed oil.

Cod Liver Oil (*Oleum Morrhuæ*, U. S. P.).—Medicinal cod liver oil should always be procured from fresh livers, by the aid of a gradually increased steam heat not exceeding 60° C. (140° F.); the oil is allowed to separate from the watery fluid, and after it has been frozen is expressed in canvas bags, whereby a pure, only slightly colored oil is obtained, the hard yellow residue, consisting of stearin and tissue, being rejected. Cod liver oil thus prepared keeps well in completely filled vessels, and when cooled to 0° C. (32° F.) should deposit no solid fats; it belongs to the drying oils, and if exposed to the air soon thickens and acquires a disagreeably strong odor and taste. The more probable adulterations of cod liver oil consist of seal oil and other fish oils, for the presence of which the Pharmacopœia gives appropriate tests.

Suet (*Sevum Præparatum*, U. S. P.).—The suet officially recognized is that obtained from the abdominal fat of the sheep, and is commonly known as mutton suet. It usually is well washed with water, then melted and strained, but still is accompanied by a peculiar, rather disagreeable odor, from which it can be freed by filtration through paper in a hot-water funnel. Suet turns rancid very readily, which can be prevented by benzoinating it.

The *National Formulary* directs that benzoinated suet (*Sevum*

Benzoinatum) be prepared by mixing benzoin in No. 40 powder with prepared suet, allowing the mixture to stand for two hours and then heating on a waterbath for one hour; after straining, the mixture may be poured into suitable moulds and allowed to congeal.

Wool Fat (*Adeps Lanæ*, U. S. P.).—The wool of sheep contains a natural grease of complex composition, which is readily removed in the process of washing the wool. If this grease be treated with weak alkalies, repeatedly washed with water, and then extracted with acetone, it yields a purified fat of yellowish-brown color and characteristic odor, and having about the same melting point as lard. This constitutes the official wool fat. It possesses the advantage over other fats of being easily miscible with large quantities of water (twice its weight) without losing its ointment-like character. When mixed with water in the proportion of 3 parts of the latter with 7 parts of wool fat, it constitutes hydrous wool fat, commercially known as lanolin, and recognized in the Pharmacopœia under the title *Adeps Lanæ Hydrosus*.

Spermaceti (*Cetaceum*, U. S. P.).—Spermaceti is obtained by expression from the fatty secretion found in the cranial cavity of the sperm whale. Before the animal is killed the fat is liquid, but afterward congeals to a yellow mass; by expression a yellow oil is removed, the residue is melted, washed with weak potassa solution and water, and finally allowed to congeal. Spermaceti is apt to become yellowish and rancid from age and when exposed to air; it melts at about 50° C. (122° F.).

Wax, White and Yellow (*Cera Alba; Cera Flava*, U. S. P.).—The only wax recognized by the Pharmacopœia is that secreted by bees, and used by them in the construction of the honey-comb. To obtain the wax, the honey is drained from the comb, which is then expressed, melted in water, and, after the impurities have subsided, run into moulds and cooled. This constitutes yellow wax, from which white wax is made by a process of sun-bleaching, as follows: Melted wax is again solidified in the form of thin ribbons or bands by allowing it to flow over wet revolving cylinders; these bands are moistened with water, and exposed to sunlight in the open air. After exposure for some time the color disappears in spots and the wax is again melted, resolidified, and treated as before, the process being repeated until the wax is completely bleached, when it is finally melted and run into moulds; besides losing its color, wax thus treated is somewhat changed by long exposure to light and air, and is more disposed to rancidity than yellow wax, as is noticeable in the modified odor. Pure yellow wax melts at 63° to 64° C. (145.4°–147.2° F.), white wax at 65° C. (149° F.); they differ from true fats in not containing glycerin, and in not forming soap when boiled with solution of alkali carbonates. Wax is completely dissolved by ether and chloroform, but not by boiling alcohol and cold benzene or carbon disulphide. Besides the crude adulterations readily observed in melted wax,

tallow and other fats, as well as vegetable wax, rosin, and paraffin, are occasionally mixed with it; they can be readily detected by the pharmacopœial tests.

Almond Oil (*Oleum Amygdalæ Expressum*, U. S. P.).—Expressed oil of almond is commercially better known as oil of sweet almond, although large quantities of the oil are obtained from the bitter almond. The yellowish color of the oil is due entirely to the colored episperm, for if blanched almonds be expressed a colorless oil will be obtained. The oil remains perfectly clear if cooled to −10° C. (14° F.), and does not congeal until a temperature of −20° C. (−4° F.) is reached. It is often adulterated with the expressed oils of apricot and peach kernels, and also other fixed oils, for which the Pharmacopœia gives appropriate tests.

Castor Oil (*Oleum Ricini*, U. S. P.).—This oil is obtained by expression from the seed of the plant popularly called palma christi, the finest quality being secured by cold expression. It differs from other fixed oils in being soluble in all proportions of absolute alcohol and in 3 times its volume of a mixture of 19 volumes of official alcohol and 1 volume of water. Castor oil is rarely adulterated.

There are at present six mills in this country where castor oil is expressed—one each in Jersey City, N. J.; Kansas City, Mo.; East St. Louis, Ill., and Memphis, Tenn., and two in St. Louis, Mo. The seed, or castor-bean, as it is called, from which the oil is expressed, is produced in the States of Illinois, Kansas, and Missouri, and in Oklahoma Territory, but the chief supply of late years has come from British India. The origin of the name castor oil is somewhat in doubt. The plant, having been introduced into the West Indies shortly after the discovery of this country, was mistaken by the Spaniards for an entirely different plant—the *Vitex angus castus*—and named by them *agno casto*, from which the English coined the word *castor* and probably applied the name to the oil.

Cottonseed Oil (*Oleum Gossypii Seminis*, U. S. P.).—The official cottonseed oil is refined bleached oil, for the crude product, obtained by hydraulic pressure from the seed, has a brown color and linseed-like odor, and contains considerable quantities of albuminous matter. After subsiding, the crude oil is treated with superheated steam, and finally well shaken with heated weak alkali solution. The yield of oil from cottonseed varies from 12.5 to 20 per cent. It congeals when cooled to 0° or −5° C. (32° or 23° F.), and is instantly colored dark reddish-brown on contact with concentrated sulphuric acid; it belongs to the drying oils, but shaken with nitric acid and water it gradually forms a colored semisolid mass. The chief use of cottonseed oil is as a substitute for more expensive fixed oils, as in the case of some of the official liniments, and at one time it was extensively employed as an adulterant for almond, olive, and other oils.

A characteristic reaction of cottonseed oil is the production of a red color if 2 mils. (or Cc.) of the oil be mixed in a test tube with 2 mils.

(or Cc.) of a mixture of equal volumes of amyl alcohol and a 1 per cent. solution of sulphur in carbon disulphide, and the tube then immersed to one-half its depth for fifteen minutes in a boiling saturated solution of sodium chloride (table salt); this is known as Halphen's test and may be used to detect the presence of cottonseed oil in other fixed oils, such as almond, olive and sesame oils.

Croton Oil (*Oleum Tiglii*, U. S. P.).—While fresh croton oil requires from 50 to 60 times its weight of alcohol for solution, the solubility increases materially with age. The oil does not congeal until cooled to —16° C. (3.2° F.). Although it belongs to the class of non-drying oils, it remains liquid if vigorously shaken with fuming nitric acid and water and then allowed to stand for one or two days; this behavior distinguishes croton oil from other non-drying oils and serves to detect adulteration with the latter.

Linseed Oil (*Oleum Lini*, U. S. P.).—Much of the linseed oil offered is expressed with the aid of heat, as thereby the yield is increased nearly 50 per cent. Like expressed oil of almond, linseed oil does not congeal until cooled to —20° C. (—4° F.). It is soluble in an equal volume of official alcohol, but becomes turbid if the proportion of alcohol is doubled. Linseed oil is one of the best drying oils known. The so-called boiled linseed oil of commerce should never be used in pharmacy.

Olive Oil (*Oleum Olivæ*, U. S. P.).—Various grades of olive oil are found on the market, the best being that commercially known as Virgin Olive Oil, which is obtained by cold expression from the flesh only of the ripe olive. It is of a pale-yellow or light greenish-yellow color, and becomes cloudy at 8° to 10° C. (46.4° to 50° F.), congealing to a whitish, granular mass at 0° C. (32° F.). Prior to 1906 much of the olive oil offered for sale was adulterated with cottonseed oil, groundnut oil, or sesame oil.

Oil of Theobroma (*Oleum Theobromatis*, U. S. P.).—This oil, better known as cacao butter, is the only official fixed oil solid at ordinary temperature. It is obtained to the extent of 40 per cent. by expression between hot plates from the roasted seeds of the cacao tree, which subsequently yield the well-known cacao mass or chocolate. While brittle at 15° C. (59° F.), it melts readily at the temperature of the human body, and for this reason is admirably adapted for use as a vehicle in making suppositories. Cacao butter is subject to adulteration with tallow, stearin, and paraffin, the presence of which can be detected by the low fusing point and the high congealing point of the oil.

Sesame Oil (*Oleum Sesami*, U. S. P.).—This oil, also known as benne oil and teel oil, is obtained to the extent of 40 to 50 per cent. by expression (preferably cold) of the seeds of the benne plant (Sesamum indicum). It is of a yellow color, somewhat darker than expressed oil of almond, almost without odor, has a bland, agreeable taste, and does not readily turn rancid. At ordinary temperature, it is thinner

than most other fixed oils, thickens at −3° C. (26.6° F.) and congeals at −5° C. (23° F.). Sesame oil belongs to the non-drying oils, and when heated to 150°–200° C. (302°–392° F.) is decolorized.

A characteristic property of sesame oil is the production of a bright red color in the aqueous layer, if 1 mil. (or Cc.) of the oil is shaken for half a minute with a solution of 0.1 Gm. of sugar in 10 mils. (or Cc.) of hydrochloric acid, the color changing to dark red on standing. This reaction is known as Baudouin's test and may be used to detect the presence of sesame oil in other higher priced oils, such as almond, olive, etc. Adulteration of sesame oil with cottonseed oil may be detected by means of the Halphen test, as stated above under cottonseed oil.

Volatile Oils.—Volatile oils are mixtures of those substances to which, in a majority of cases, the peculiar odors of plants are due. Although the attribute volatile is indicative merely of a physical property which most of these substances have in common, and in nowise refers to their source, the designation volatile oil has been restricted entirely to volatile products from the vegetable kingdom. In recent years the term has been made to include artificial substances identical with, or at least closely related to, such natural plant products. Volatile oils do not all preëxist in the plant, some being the result of fermentative action between certain constituents of the plant in the presence of water and others being produced by destructive distillation. Volatile oils may exist in every part of the plant from the root to the seed, and when several oils are present in different parts of the same plant they will generally be found to differ in physical as well as chemical properties; as, for instance, the oils of orange obtained from the leaf, flower, and rind. Volatile oils usually occur in separate cells, as glands in the herbaceous portion and rinds of many fruits, or distributed throughout the interior tissue, or forming distinct oil tubes, as in the fruit of fennel, anise, etc. The odor of volatile oils, while in some instances due to their particular composition, in others appears to be due to atmospheric influences, since oil of turpentine and other oils when rectified in an atmosphere of carbon dioxide have been found devoid of all unpleasant odor, and yet, when again exposed to the air, they soon acquired their characteristic odor. With few exceptions, volatile oils are lighter than water, and their solubility in water is very variable; their specific gravities at 25° C. (77° F.) range from 0.845 to 1.180. Absolutely pure volatile oils are colorless, but the commercial varieties are frequently colored yellow, green, blue, red, and brown; the color in most instances disappears when the oil is brought into solution. Many volatile oils are completely soluble in glacial acetic acid, and all are soluble in alcohol, but in proportions varying from less than an equal volume to ten volumes or more. They have but few properties in common with fixed oils, but like these are soluble in ether, chloroform, and carbon disulphide. Freshly prepared volatile oils are generally freely soluble in benzin, but after exposure they gradually lose this property, and often form turbid mixtures when shaken with the same.

When dropped upon filter paper they cause a stain somewhat resembling that of fixed oils, but which is dissipated upon the application of heat; the stain produced by old or partly resinified volatile oils frequently cannot be removed by heat, but can be readily distinguished from the stain of fixed oils by its shining, varnish-like appearance and by its complete removal with the aid of warm alcohol, the stain from fixed oils being devoid of luster and insoluble in alcohol. Volatile oils are inflammable, and burn with a bright but sooty flame; exposed to air and light they are more or less rapidly oxidized, being gradually converted into a viscid oil, and finally even into a solid resin. They never become rancid in the sense mentioned under fixed oils, and do not contain glycerin. Owing to the changes which volatile oils undergo through exposure to light and air, they should be preserved in well-stoppered bottles in a dark place; amber- or yellow-colored glass is best adapted for oil containers, as it intercepts the actinic rays of light. The addition of deodorized alcohol or Cologne spirit will also preserve the fine aroma of such oils as lemon and orange, not more than 5 per cent. by volume being necessary. Resinfied oils may be restored by redistillation with water or weak alkali, or, if in small quantities, by Cuvier's method, which consists in shaking the oil for fifteen or twenty minutes, with a magma formed of animal charcoal and a solution of borax, whereby the resinified portion is united to the borax and the oil becomes limpid. The whitening of corks in bottles containing volatile oils is due to the presence of ozone produced by the gradual oxidation of the oil.

The adulterations to which volatile oils are subjected are fixed oils, alcohol, and highly rectified petroleum; frequently also, the higher priced oils are mixed with cheaper and inferior oils. Fixed, oils are easily detected by a permanent greasy stain upon paper, and by a non-volatile residue when the suspected oil is subjected to distillation. Alcohol may be tested for in several ways. If the oil be shaken in a graduated tube with an equal volume of water or glycerin, and then allowed to stand at rest, any diminution in the volume of the oil would indicate alcohol, and approximately also the proportion present; if considerable alcohol be present, the characteristic lambent blue flame of burning alcohol will be observed if a portion of the suspected oil is ignited in a dark room; fused calcium chloride and dry potassium acetate are insoluble in volatile oils, but in the presence of alcohol become soft and even liquid, depending upon the proportion of alcohol; potassium acetate and sulphuric acid added to volatile oils will generate acetic ether if alcohol be present, which may be detected by its odor; and aniline-red is insoluble in pure volatile oils, but colors these red in the presence of alcohol. Adulterations with rectified petroleum are often not easily detected, and may require a careful chemical examination; for it, as well as for the inferior volatile oils, the Pharmacopœia prescribes appropriate tests under the head of the respective oils likely to be thus contaminated.

The usual method of obtaining volatile oils is by distillation. In some of the Asiatic countries, where the world's supply of a few volatile oils is still obtained, rather crude methods prevail even at the present time. Thus the plan is followed of using wooden cylindrical stills provided with a perforated diaphragm or false bottom, as shown

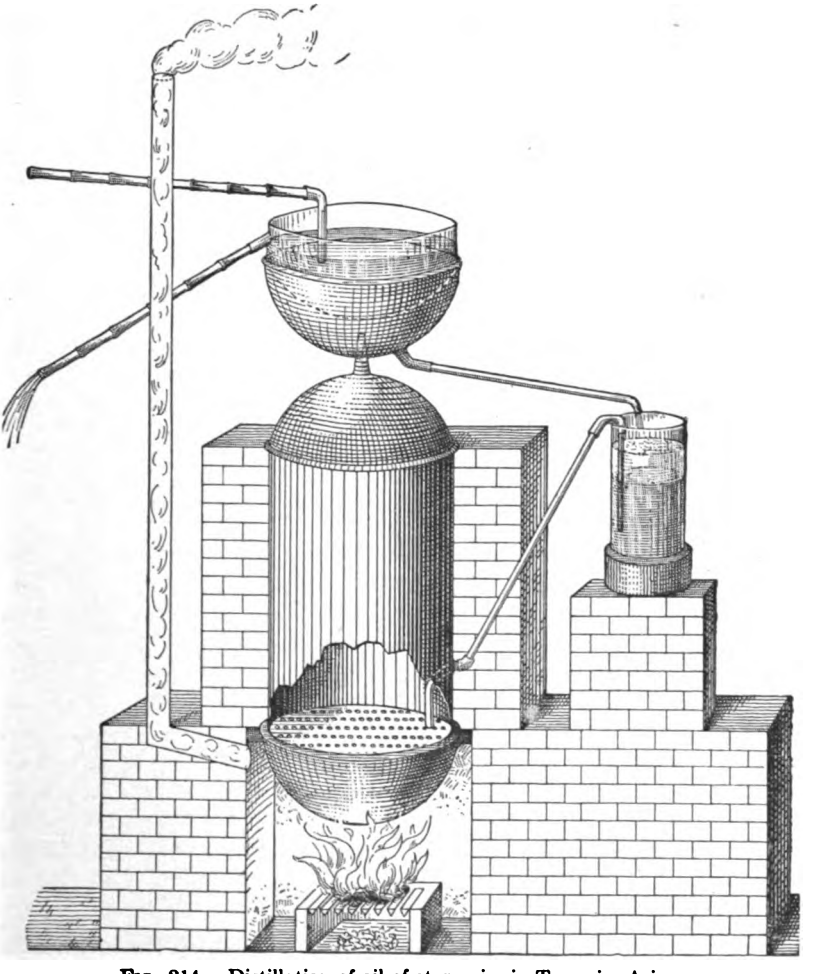


FIG. 214.—Distillation of oil of star-anise in Tonquin, Asia.

in Fig. 214, on which the oil-yielding material is placed, water being put into the boiler on which the still rests and direct heat applied until the water boils, and the boiling continued as long as the distillate shows the presence of volatile oil. As shown in the illustration, the vapors are condensed in the cup-shaped condenser above the still, and flow from there into a suitable receiver, made of wood and lined

with tin, whence the watery portion of the distillate flows back into the still, while the oil rises to the surface and is removed when a sufficient quantity has collected. In Fig. 215 may be seen the peculiar arrangement of a wooden still with tin condenser for the distillation of oil of cassia cinnamon. The still, as in the preceding case, is provided with a perforated bottom and rests upon an iron boiler placed directly over the firepot of a brick furnace. The distillate collects in a gutter near the bottom of the cylindrical condenser and flows from there into earthenware receivers. Oil of cinnamon being heavier than water,

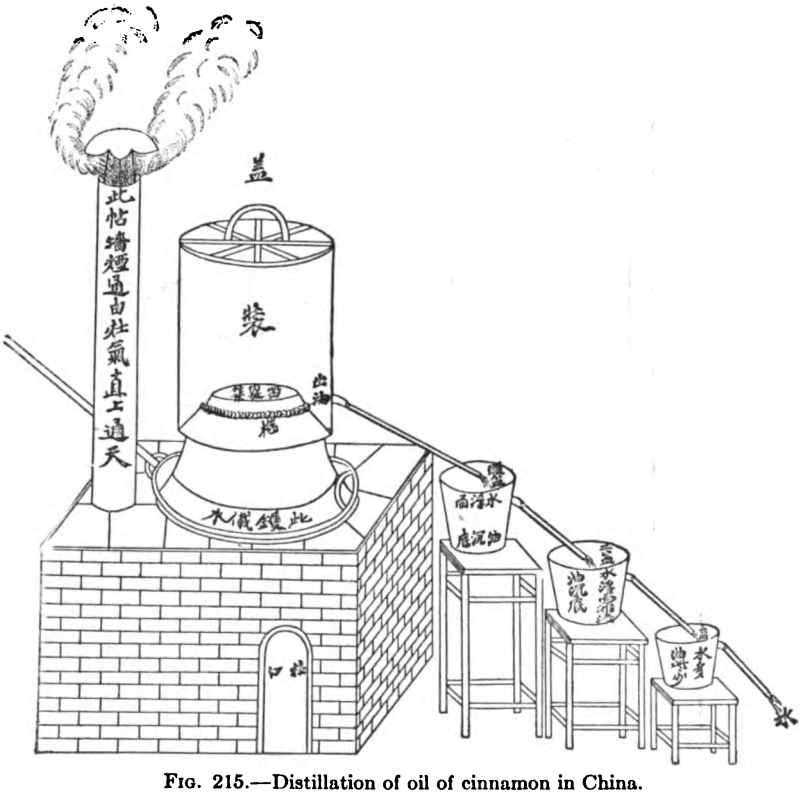


FIG. 215.—Distillation of oil of cinnamon in China.

the distillate is collected in a series of vessels in which the oil sinks to the bottom and the aqueous portion flows into another vessel, to be again used in a subsequent distillation. A still cruder apparatus, in use as recently as 1894, is shown in Fig. 216. It is used for the distillation of oil of cajuput, and consists of a wooden cask, *a*, into which are placed the leaves of the melaleuca plant and some water, and which is heated by means of a rudely constructed fireplace. The vapors are carried through the tin still-head *b* by means of a tube into the second cask *c*, which is kept supplied with cold water running in through

the tube *d*, made of bamboo, where they are condensed and flow through a funnel-shaped device, made of cocoanut shell, into a bottle. The oil and water gradually separate, the oil rising to the surface and the water flowing into the tub *e* through a small hole near the bottom of the bottle.

Although the boiling points of volatile oils are considerably above that of water, the oils pass over rapidly with the vapor of boiling water, and in the leading establishments in this country and Europe volatile oils are now distilled by passing steam under pressure into stills which contain the material on a series of perforated trays extending across the inner body of the still; by this method compaction is avoided, the steam can readily penetrate every particle of the material, and a

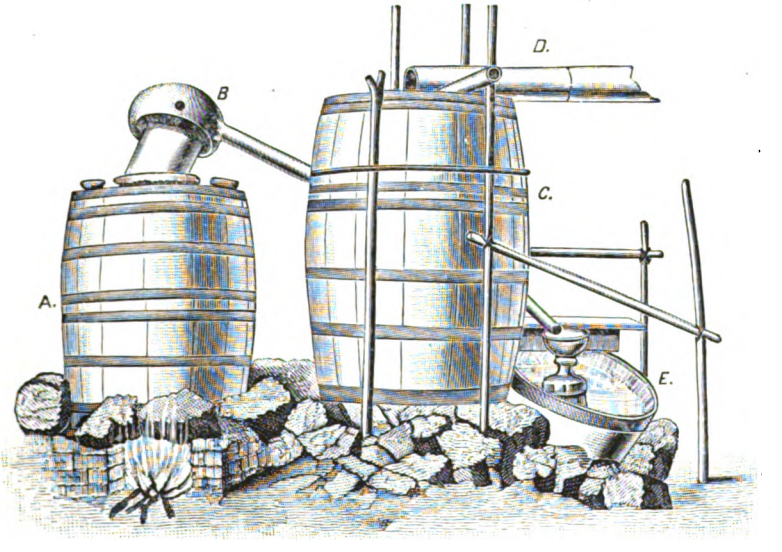


FIG. 216.—Distillation of oil of cajuput in the Molucca Islands.

much finer quality of oil results, since prolonged contact with boiling water has a deleterious effect upon many oils. Fig. 217 represents the interior of a modern establishment for the distillation of volatile oils by steam, as carried on by Messrs. Schimmel & Co., at Leipzig, Germany, to whom the author is indebted for the loan of this and other illustrations shown in this chapter. Whenever the volatile oil is deeply imbedded in the material, as in the case of cloves, cubebs, and many barks and seeds, it is necessary that this first be reduced to a coarse powder so as to facilitate the liberation of the oil. The distillate, which is a mixture of oil and water, is collected in suitable receivers, either in the form of Florentine flasks with a single outlet tube near the bottom and reaching nearly to the top, as shown in Fig. 218, or of tall cylinders provided with two tubes, a long one near

the bottom and a short one near the top; as the distillate cools, it separates into two distinct layers, one consisting of pure oil and the other of water holding some oil in solution and suspension, which is

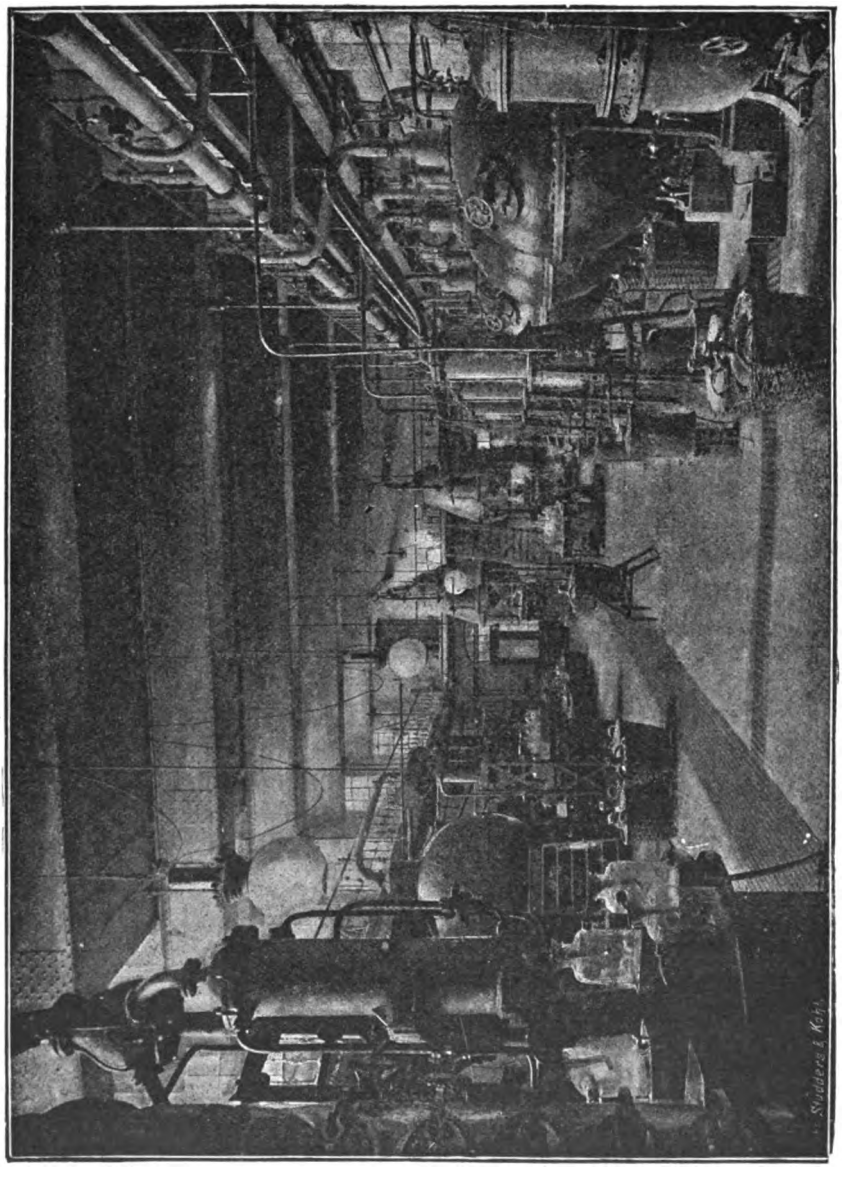


FIG. 217.—Modern distillation of volatile oils by steam.

subsequently regained, either by conveying the water back direct to the still or by distilling the water in separate stills, frequently after the addition of table salt to facilitate separation of the oil. As a rule,

the layer of oil floats on top, except in those cases in which the oil has a specific gravity above 1.000, as the oils of cloves, cassia, gaultheria, etc. The lower layer will flow off through the long tube as soon as the liquid in the flask or cylinder reaches the height of the curve in the tube, and will continue to flow as long as distillation continues. When the upper layer fills the vessel, the latter must be changed; or if it is provided with two tubes, as shown in Fig. 219, the liquid will pass out through the short tube into another receptacle; thus the two layers of liquid are withdrawn simultaneously almost as fast as separation takes place.

The contrast between modern distillation of volatile oils by steam and former crude methods still practiced in some countries, is strikingly shown in the two illustrations representing the distillation of oil of rose. Fig. 220 represents a complete steam plant for distillation of the oil, at Leipzig, Germany, from flowers grown in the near-by

FIG. 218.—Florentine flask for collecting volatile oils.

FIG. 219.—Receiver for volatile oils with two outlets.

districts. In Fig. 221 is shown the arrangement of a copper still extensively used by the Bulgarians at the present time, which is capable of accommodating a charge of about 22 pounds of freshly gathered roses and 20 gallons of water.

Besides distillation, other methods are employed for obtaining volatile oils, such as expression by hand or machine, and extraction by means of suitable solvents; for certain flowers possessing delicate fragrance, such as the violet, heliotrope, mignonette, tuberose, etc., which do not contain volatile oils in appreciable quantities, the treatment with fats by maceration and digestion, or the pneumatic process, is resorted to for obtaining the odorous principles.

Expression is particularly suited for those oils contained in the epidermal cells of the fruit, as in the natural order Aurantiaceæ, and yields oils of superior quality; the oils of orange and lemon are very sensitive to heat; and hand pressed oils always command a higher

price on account of their delicate aroma. A special apparatus, known as *écuelle à piquer* (a pricking basin) (see Fig. 222), is extensively employed in Southern France; it consists of a tin basin about 8 inches

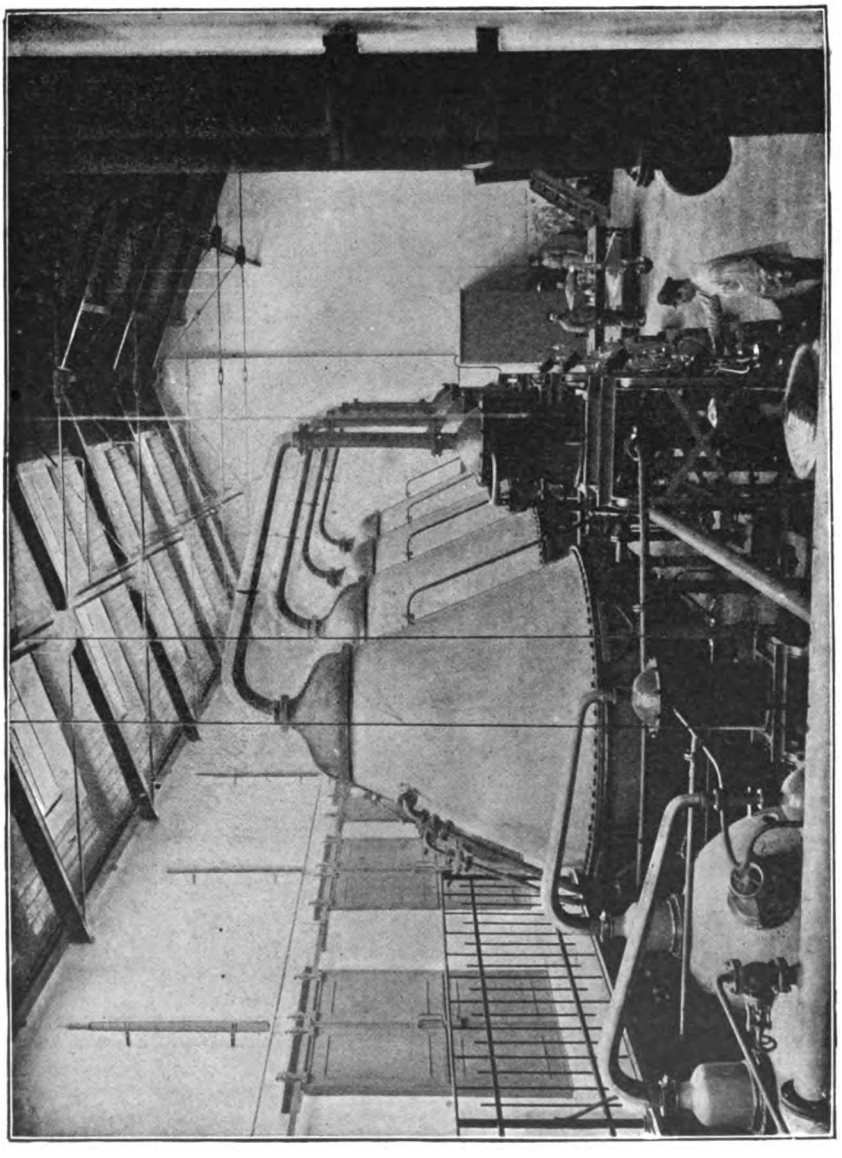


FIG. 220.—Modern apparatus for the distillation of oil of rose.

in diameter, studded with numerous (150) short, pointed brass needles, and provided with a hollow handle. The operator holds the basin in one hand and with the other, while rotating the fruit, he continually

presses it against the needle points, thus rupturing the oil cells and causing the oil to flow into the handle, whence it is transferred to larger vessels and allowed to separate from any fruit juice with which it has become contaminated. Another method of hand pressing is

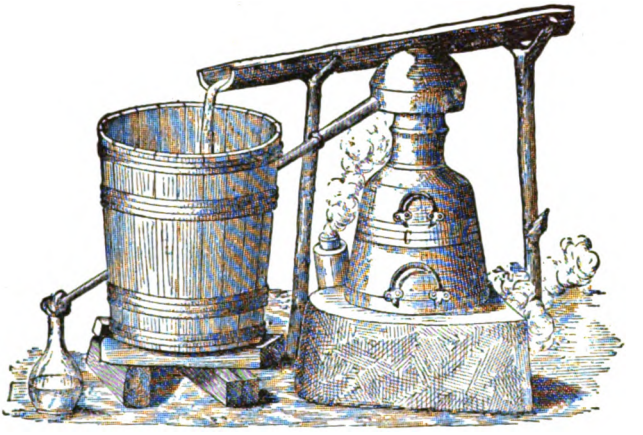


FIG. 221.—Distillation of oil of rose in Bulgaria.

practised in Italy, known as the sponge method; the rind of the fruit is separated from the pulp and cut into three or four strips, which are held over a sponge and expressed by convex flexion, whereby the cells are burst and the oil is ejected. When the sponge has become saturated with oil it is expressed into an earthen vessel. The residual rind is frequently mixed with water and again expressed in linen sacks, to yield a lower grade of oil.

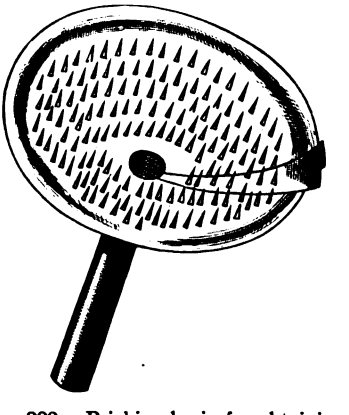


FIG. 222.—Pricking basin for obtaining hand pressed volatile oils.

The solvents employed for the extraction of volatile oils are petroleum benzin, ether, carbon disulphide, acetone, etc., solution being effected in tightly closed apparatus by means of maceration and percolation. After complete extraction of the volatile oil the solvent is recovered by distillation at temperatures not affecting the oil, and the residue must then be further purified by rectification. The chief drawback to this method is the possible extraction of other substances besides volatile oils, such as resin, fat, etc., which are sometimes eliminated with great difficulty; hence it is not employed to any great extent.

The process of maceration is confined to the extraction of delicate odors from flowers, and belongs more properly to the art of perfumery than to pharmacy; although the odors are quite marked and persistent, the volatile oil in many flowers is present in such small quantity that it cannot be recovered by distillation, and in some cases is injured by even moderate heat. Complete absorption of the odorous principle by fats in the cold is practised on a large scale in France, where the process is known as *enfleurage;* bland, inodorous fats, such as purified lard, tallow, olive oil, benne oil, and cottonseed oil, being used for the purpose. In the last three cases the flowers are left in contact with the oil in closed vessels for some time and then strained. When solid fats are used, they are spread thinly on plates of glass, and then covered with flowers, which are renewed from time to time as long as the fat continues to absorb the odor. The fats, impregnated with the odor of the flowers, are finally scraped from the glass, and constitute the well known French pomades so extensively employed in the manufacture of fine perfumery. In order to extract the odor, the pomade is repeatedly shaken (washed) with deodorized alcohol, and the solution exposed to cold in special cylinders, called crystallizers, whereby all trace of fat is removed.

The pneumatic method consists in passing a current of air into a vessel filled with fresh flowers, whereby the air becomes laden with perfume, and is then passed into another vessel containing fat in a fine state of division, so that intimate contact between the air and fat is effected, and thus the odor is transferred to the fat.

Very few volatile oils are of simple composition, and some are known to contain even six or eight distinct bodies. While formerly many arbitrary and erroneous notions were entertained regarding the nature of volatile oils, much light has been shed upon their true character by Wallach and others during the past 25 or 30 years.

Volatile oils may be conveniently divided into groups for the purpose of facilitating classification and better study of general properties. Thus, Group 1 comprises the simple hydrocarbon oils, and to this group the name terpenes is generally applied; Group 2 comprises oils composed of variable mixtures of hydrocarbons and their oxygen derivatives, a few of the oils even consisting entirely, or very nearly so, of such oxygen compounds; Group 3 embraces a small number of oils characterized by the presence of sulphur derivatives; Group 4 comprises the empyreumatic oils, or those obtained by destructive distillation.

The chemical character and composition of volatile oils will be considered further on, when the student's knowledge of chemistry will better fit him for a proper understanding of the subject.

Group 1.—The hydrocarbon oils are the simplest volatile oils known, being composed of carbon and hydrogen only, and are derived mainly from the natural orders Coniferæ, Leguminosæ, and Piperaceæ. They are divided into hemiterpenes, terpenes, sesquiterpenes, diter-

penes, etc. Some of these are frequently found present also in members of the other groups. The terpenes proper occur in five isomeric forms (having the same centesimal composition, but different properties), known as *pinene, dipentene, limonene, sylvestrene* and *phellandrene;* of these, sometimes two or three are found associated in the same oil. As a class, the hydrocarbon oils are the least soluble in alcohol and water, and have specific gravities ranging from 0.850 to 0.900. They readily become resinified when exposed to the air, and when left in contact with alcohol and nitric acid gradually absorb water and yield crystallizable compounds. They react violently with iodine, and are converted into a hard resinous mass by nitric acid.

Some well known members of this class are oil of copaiba, oil of cubeb, oil of erigeron, oil of juniper, and oil of turpentine.

Group 2.—These oils, as stated above, contain oxygen derivatives of hydrocarbons, and are composed of variable mixtures of terpenes and other bodies, such as alcohols, aldehydes, ethers, acids, ketones, phenols, etc., which can be separated by fractional distillation. They are widely diffused in plants; the larger number are derived from the natural orders Umbelliferæ, Labiatæ, Lauraceæ, Myrtaceæ, and Compositæ. The majority of oils belonging to this group are soluble in an equal volume of alcohol or glacial acetic acid, and many are soluble in these two liquids in all proportions They are far more soluble in water than are the simple terpenes, and hence are largely used in the preparation of medicated waters. Decreased solubility in alcohol, or in a mixture of alcohol and water, is frequently made a test for adulteration with hydrocarbons and other oils.

While nearly all the oils containing oxygen derivatives of the hydrocarbons are lighter than water, a few will sink when dropped into water, the highest specific gravity for volatile oils being found in this class, namely, 1.180 at 25° C. (77° F.). Some, owing to their peculiar chemical composition, form a solid mass when shaken with an equal volume of concentrated potassa or soda solution, while others show a similar reaction with sodium bisulphite. Upon exposure to low temperatures some of the oils of this class thicken, and even congeal to a solid mass, which property is utilized as a test for their quality. The value of these oils lies, as a rule, in the oxygen compounds which they contain, and which are present in the different oils in proportions varying from 3 to 90 per cent. and over. It has been possible, by synthetic methods, to produce artificial oils practically identical with the natural, of which the official methyl salicylate or artificial oil of wintergreen (identical also with the natural oil of sweet birch) is an example. The Pharmacopœia recognizes a single concrete volatile oil—camphor—which has been appropriately placed among the oils of this group, since its chemical composition shows it to be a ketone.

The official members of Group 2 are the oils of anise, cajuput, caraway, cloves, chenopodium, cinnamon, coriander, eucalyptus, fennel,

lavender flowers, lemon, orange flowers, orange peel, peppermint, spearmint, nutmeg, pimenta, rosemary, santal, sassafras, and thyme.

Some plants do not produce volatile oils in nature, but contain certain principles which, in the presence of water, react upon each other, causing the formation of new compounds, one of which is a volatile oil; such is the case with certain plants belonging to the natural order Rosaceæ, suborder Amygdalæ. The name nitrogenated oils was formerly given to this class because in their formation they are always accompanied by a substance containing nitrogen, hydrocyanic acid, which is present in variable proportion and which gives to the oils their poisonous character. The only official oil belonging to this subclass is the oil of bitter almond, which is prepared by mixing freshly powdered bitter almonds with the residue left after expressing the fixed oil from bitter and sweet almonds, adding water, and distilling at a moderate heat. The specific gravity of the oil ranges from 1.045 to 1.060 at 25° C. (77° F.), and that of the purified oil is about 1.032. Bitter almonds, as well as peach and apricot seeds, contain both the albuminous ferment and the peculiar compound amygdalin, necessary for the reaction; while sweet almonds contain only the ferment, and hence will yield no volatile oil unless mixed with the bitter variety. The bulk of "oil of bitter almond" is no doubt now obtained from apricot and peach seeds. The hydrocyanic acid present in oil of bitter almond sometimes amounts to as much as 6 or 7 per cent., and may be removed by shaking the oil with ferrous chloride and lime water and then rectifying by distillation. Oil of bitter almond is soluble in 300 parts of water and in all proportions of alcohol.

Group 3.—The oils belonging to this group, as in the preceding group, are the result of fermentative action, in which the living plant takes no part except to provide the necessary active principles for the subsequent reaction in the presence of water. Sulphur is present in the oils, combined with certain organic radicals, in the form of sulphide or sulphocyanate. Nearly all the oils of this class are obtained from members of the natural order Cruciferæ. The Pharmacopœia recognizes but one volatile oil containing sulphur, namely, the volatile oil of mustard, made from black mustard seed, which has a specific gravity varying from 1.013 to 1.020 at 25° C. (77° F.).

Group 4.—Among the products of destructive distillation are certain volatile oils which are characterized by a peculiar tarry odor, and acid reaction and a somewhat bitter taste, and known as empyreumatic oils. They are lighter than water, and sparingly soluble in this liquid, but readily soluble in alcohol. Oil of cade and oil of tar are the only empyreumatic oils recognized in the Pharmacopœia; the former is obtained by the dry distillation of the wood of the prickly cedar (Juniperus oxycedrus) and the latter by distillation of tar.

PART II.

PRACTICAL PHARMACY.

THE study of practical pharmacy involves both galenical and extemporaneous pharmacy, the former pertaining to the various preparations of drugs, the latter to the many operations of the dispensing counter. The different classes of plant products used in medicine, as well as the various methods of solution and separation, have been considered in previous chapters; the numerous preparations of drugs will be treated after a plan which, for a number of years, has proved satisfactory to students, and although not based on a strictly symmetrical arrangement, is probably in keeping with the advance made by them in other branches of study up to this point.

The official preparations may be divided into those of a strictly pharmaceutical character and those involving chemical action; the latter class will be considered under the head of pharmaceutical chemistry, where the preparations of each element or compound will be grouped together.

The galenical preparations of the Pharmacopœia may be classified as follows: (1) Waters; (2) Solutions or Liquors; (3) Decoctions and Infusions; (4) Syrups; (5) Mucilages, Honeys, and Glycerites; (6) Elixirs; (7) Spirits; (8) Tinctures; (9) Wines and Vinegars; (10) Fluid Extracts; (11) Extracts; (12) Oleoresins and Resins; (13) Collodions; (14) Emulsions; (15) Mixtures; (16) Pills; (17) Lozenges and Confections; (18) Powders and Triturations; (19) Granular Effervescent Salts; (20) Cerates and Ointments; (21) Liniments and Oleates; (22) Plasters and Suppositories.

The operations of the dispensing counter are intimately associated with the various preparations of drugs officially recognized, and, instead of treating them separately under a special head, it has been thought most convenient to consider them in connection with some of the subdivisions named above, particularly as eight classes of the official galenical preparations require remarks and explanations which apply equally to the details of dispensing pharmacy. Certain forms of administering medicines, not as yet recognized in the Pharmacopœia, but which of late years have come into use extensively, such as Compressed Tablets, Tablet Triturates, Hypodermic Tablets, Medicated Disks, etc., may be looked upon as modifications of the official class of lozenges and studied in connection with these.

CHAPTER XIII.

THE OFFICIAL WATERS.

THE official waters include common and distilled water, as well as those known as medicated waters; all the latter are solutions of volatile substances, and were it not for this pharmaceutical classification two of them might be considered as more appropriately belonging to the class of liquors or solutions proper, instead of medicated waters, namely, *aqua ammoniæ* and *aqua ammoniæ fortior*.

The U. S. Pharmacopœia directs three different methods for the preparation of medicated waters, namely, by simple agitation of the medicinal ingredient with recently boiled distilled water, by trituration of essential oils with purified talc or purified silicious earth (Kieselguhr) and recently boiled distilled water, and by distillation. In England and Germany the second method is not practised, the pharmacopœias of both countries directing all aromatic waters to be made by distillation.

The most important of the official waters is undoubtedly distilled water, because it is intended to be free from impurities, inorganic as well as organic, and is the only kind that should be used in making aromatic waters. River water and most spring waters contain in solution varying quantities of mineral compounds, and frequently carbon dioxide and organic matter, which render the water unfit for many pharmaceutical purposes; boiling and subsequent filtration through sand and charcoal will improve the water, but do not remove the salts held in solution, which if present in appreciable quantity will cause precipitation if silver nitrate or lead acetate be dissolved in the water. The so-called hardness of water may be due to the presence of calcium sulphate, and is then known as permanent hardness, or it may be due to calcium carbonate held in solution by an excess of carbon dioxide, which is always the case with spring water coming from limestone districts; boiling such water expels the excessive carbon dioxide, causing the lime salt to be precipitated, whereby it is rendered soft. The directions of the Pharmacopœia to reject the first 10 per cent. of the distillate and to collect only 75 per cent. for use, are for the purpose of getting rid of the gases and volatile compounds always present in water, and to avoid the decomposition products from ammonia compounds and organic matter, with which the last portions of water in the still are likely to be contaminated.

In the manufacture of distilled water all contact with iron and lead

should be avoided, and either glass or pure tin apparatus used, especially for the condensation of the vapors. The occasional appearance of confervæ (microscopic plants) in distilled water is due to the presence of minute spores derived from the air, and may be prevented by keeping it in vessels so arranged that the air can enter only after having passed through a layer of cotton.

The Pharmacopœia also gives official recognition to sterilized distilled water (*Aqua Destillata Sterilisata*), which is to be obtained by transferring a convenient quantity of freshly distilled water to a previously cleansed and sterilized flask, closing the mouth of the flask with a pledget of sterilized cotton and then boiling the contents vigorously for thirty minutes; the water is allowed to cool without removing the cotton, the mouth of the flask and the cotton being finally covered with sterile parchment paper.

The following classification of the official waters shows at a glance their strength and mode of preparation:

OFFICIAL WATERS MADE BY AGITATING THE MEDICINAL INGREDIENT WITH RECENTLY BOILED DISTILLED WATER.

Latin name.	English name.	Composition.
Aqua Amygdalæ Amaræ U. S. P.	Bitter Almond Water	1 mil. (or Cc.) Oil of Bitter Almond, 999 mils. (or Cc.) of Distilled Water.
Aqua Aurantii Florum U. S. P.	Orange Flower Water.	Equal volumes of stronger Orange Flower Water and Distilled Water.
Aqua Chloroformi U. S. P.	Chloroform Water	A saturated solution of Chloroform in Distilled Water. It contains about 5 mils. (or Cc.) of Chloroform in 1000 mils. (or Cc.) of the solution.
Aqua Creosoti U. S. P.	Creosote Water	10 mils. (or Cc.) of Creosote and 990 mils. (or Cc.) of Distilled Water.
Aqua Rosæ U. S. P.	Rose Water	Equal volumes of stronger Rose Water and Distilled Water.

Under the title Aqua Phenolata—Phenolated Water (Carbolic Acid Water, Carbolated Water), the National Formulary recognizes a solution of official liquefied phenol in distilled water.

Bitter almond water contains variable quantities of hydrocyanic acid, derived from the oil, as the latter is required by the Pharmacopœia to contain not less than 2 per cent. nor more than 4 per cent. of the acid; it is a weak and rather uncertain preparation. The German Pharmacopœia directs that bitter almond water shall be made by distillation and shall contain 0.1 per cent. of absolute hydrocyanic acid, which corresponds in strength to the distilled cherry laurel water of the British Pharmacopœia.

OFFICIAL WATERS MADE BY PASSING GASES THROUGH WATER.

Latin name.	English name.	Strength.
Aqua Ammoniæ U. S. P.	Ammonia Water	10 per cent. by weight of gaseous Ammonia.
Aqua Ammoniæ Fortior U. S. P.	Stronger Ammonia Water	28 per cent. by weight of gaseous Ammonia.

OFFICIAL WATERS MADE BY TRITURATING THE MEDICINAL INGREDIENTS WITH PURIFIED TALC AND THEN MIXING WITH RECENTLY BOILED DISTILLED WATER AND FILTERING.

Latin name.	English name.	Composition.
Aqua Anisi U. S. P.	Anise Water	2 mils. (or Cc.) of Oil of Anise and 998 mils. (or Cc.) of Distilled Water.
Aqua Camphoræ U. S. P.	Camphor Water	8 Gms. of Camphor in 1000 mils. (or Cc.) of finished product.
Aqua Cinnamomi U. S. P.	Cinnamon Water	2 mils. (or Cc.) of Oil of Cinnamon and 998 mils. (or Cc.) of Distilled Water.
Aqua Fœniculi U. S. P.	Fennel Water	2 mils. (or Cc.) of Oil of Fennel and 998 mils. (or Cc.) of Distilled Water.
Aqua Menthæ Piperitæ U. S. P.	Peppermint Water	2 mils. (or Cc.) of Oil of Peppermint and 998 mils. (or Cc.) of Distilled Water.
Aqua Menthæ Viridis U. S. P.	Spearmint Water	2 mils. (or Cc.) of Oil of Spearmint and 998 mils. (or Cc.) of Distilled Water.

With the exception of camphor water, this whole class is prepared by triturating the oil with about 8 times its weight of purified talc, after which the distilled water is gradually added with continued trituration; the mixture is finally filtered through paper. Thorough trituration with an insoluble powder causes division of the oils into minute particles, in which condition they are more readily dissolved by water. In the case of camphor water, 8 Gms. of camphor are dissolved in 8 mils. (or Cc.) of alcohol, and then triturated with 15 Gms. of purified talc until the alcohol has evaporated, after which the preparation is finished like the others. It is important that the purified talc be not used in the form of an impalpable powder, as this is apt to pass through the filter and necessitate frequent refiltration, but a coarser powder, about No. 60, should be employed. Permission is also given in the Pharmacopœia to effect solution of the volatile oil by replacing the purified talc by pulped or shredded filter paper, or by the addition of oils to hot water and separation of the excess of the former after active agitation and subsequent cooling of the mixture, or by distillation of the drug or oil with water. When shredded filter paper is used, the best plan is to drop the oil upon the shredded paper, add this to the hot distilled water contained in a strong bottle or jug, and shake actively until the liquid is cold, after which a perfectly clear solution may be obtained by simple filtration. In the author's experience this method produces excellent results with little labor. The use of alcohol for the purpose of facilitating solution of the oil

in the water must be condemned as liable to cause trouble, the very weak alcoholic liquid having a tendency to become sour through oxidation under favorable conditions. Calcium phosphate, directed in the U. S. P., 1890, is not a good medium for division of the oils, and is frequently found impure from contamination with soluble matter. Magnesium carbonate, at one time largely used, is not desirable, as it is not wholly insoluble, and this fact has often given rise to trouble, as in the case of cinnamon water, which invariably has a yellow color when made with this agent, and in the case of mixtures of medicated waters with lime water, producing turbidity.

OFFICIAL WATERS MADE BY DISTILLATION.

Latin name.	English name.	Strength.
Aqua Aurantii Florum Fortior U. S. P.	Stronger Orange Flower Water	Saturated.
Aqua Destillata U. S. P.	Distilled Water	Absolutely pure
Aqua Hamamelidis U. S. P.	Hamamelis Water	Saturated.
Aqua Rosæ Fortior U. S. P.	Stronger Rose Water	Saturated.

Aromatic waters made by distillation possess in many instances a more agreeable flavor than the aqueous solution of the corresponding volatile oils, which is probably due to the fact that, besides the volatile oil, other volatile compounds, such as acids, or ethers, are present in the drug, and, passing over with the steam, remain dissolved in the condensed water. In distilling aromatic waters over a naked fire care should be taken to prevent the material from being scorched, which can be obviated by placing the drug either upon a diaphragm or in a perforated vessel or wire cage, and then suspending this in the water. A peculiar odor is observed in some waters immediately after they have been distilled and condensed in tin vessels, but not when glass vessels have been used; if the waters be exposed to the air in loosely stoppered vessels for a few days, this still odor disappears and the natural odor of the water becomes apparent.

The *stronger* orange flower and rose waters are obtained, on a large scale by distilling the fresh flowers respectively of the bitter orange (*Citrus Aurantium amara*) and of the hundred-leaved or pale rose (*Rosa centifolia*) with water; in commerce they are distinguished as of *triple* or *quadruple* strength. In order to produce a saturated solution of the oil, recourse is had to the process of *cohobation* or redistillation, which consists in distilling the same water two or three times with fresh portions of the flowers.

Distilled hamamelis water, commercially better known as *distilled extract of witch hazel*, or simply *extract of witch hazel*, represents a saturated aqueous distillate obtained by distilling with steam or water the bark, twigs and smaller stems of hamamelis collected in the fall, and adding 150 milliliters of alcohol to each 850 milliliters of distillate. It should contain not less than 14 per cent. of alcohol and possesses a characteristic odor and taste. The Pharmacopœia demands the

absence of formaldehyde and metallic impurities and gives appropriate tests for their detection.

For the preparation of distilled water a special apparatus has been put upon the market, which is said, by those who have used it, to yield an exceptionally pure water and in considerably larger quantity than is usually expected from a still of like size. The apparatus, which is illustrated in Fig. 223, is known as the Curran water still, and can be used anywhere if gas and constant water supply be available.

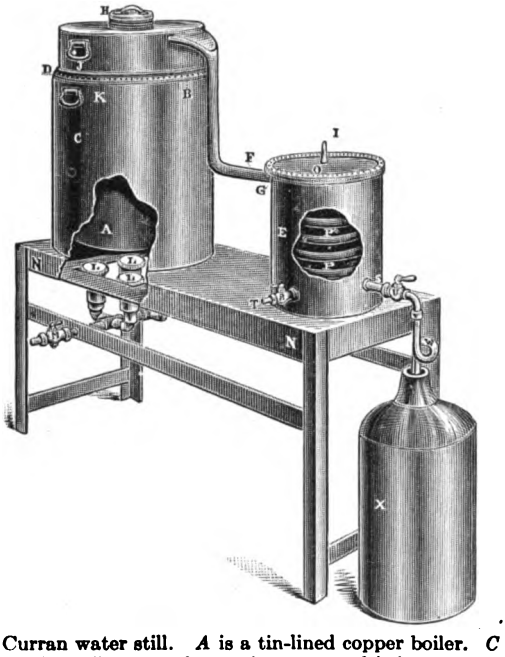


FIG. 223.—The Curran water still. *A* is a tin-lined copper boiler. *C* is a galvanized jacket for supporting the boiler over the gas burners, and it is attachable at *B*, *B;* it is also intended to act as a flue to utilize the heat from the gas-burners on the sides of the boiler. *H* is a screw cover removable for filling or cleansing the boiler. *F* is the vapor-pipe from the boiler to the condensing coil, *P*, in the galvanized iron condensing tank. *E*, which is provided with an inlet for cold water at *T*, and an outlet for warm water at *I*. At *G* is a union for connecting the vapor pipe with the condensing coil. *S*, is the outlet for the condensed water, and *X* is the receiving vessel. *J* is a perforated ring resting on the jacket, and *K* are vent holes in the ring through which the exhausted gases pass off. *O* is a removable cover for cleansing the condensing tank. *R* is a faucet for drawing off the water from the condensing tank. *L*, *L*, *L*, are the gas burners, and *N* the iron frame supporting the apparatus and burners. *M* is a gas cock for regulating the supply of gas to the burners.

The tin-lined copper boiler has a capacity of 6 gallons, and from it 4½ gallons of distilled water can be obtained in about two and a half hours; this allows the first quart of distillate, carrying with it all volatile matter, to be rejected, and also retains a quart of water in the boiler. The rapid vaporization of the water in the boiler is effected by means of four rose burners consuming jointly about 25

cubic feet of gas per hour, the generated heat being all utilized on the bottom and sides of the boiler, which is surrounded by a galvanized iron jacket, as shown in the illustration. The vapor pipes passing from the boiler, and the condensing coil, are both heavily lined with pure block tin, thus avoiding contact of the water with any other metal. There is no pressure on any part of the apparatus, the vapor being condensed as fast as generated and the distillate passing rapidly into the receiving vessel. Larger sizes of the Curran water still are made

FIG. 224.—Stokes automatic water still.

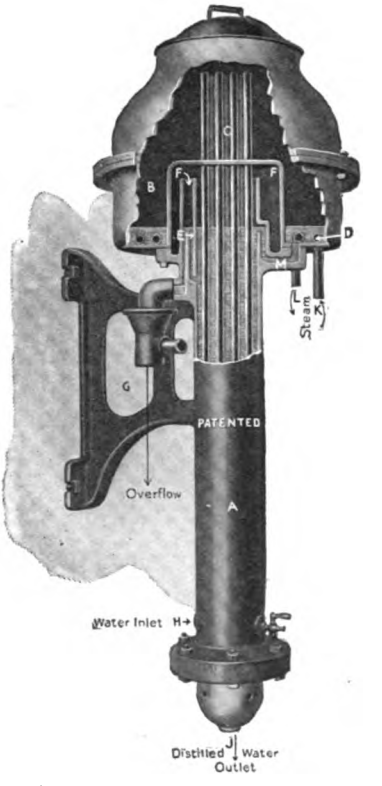


FIG. 225.—Automatic water still (sectional view).

for use with gas or coal, delivering, according to the manufacturers' statements, which are guaranteed, from 4 to 10 gallons of distilled water per hour.

In large manufacturing establishments, where distilled water is in great demand and constant supply of steam available, use is made of large automatic stills. Fig. 224 represents an automatic still manufactured by the F. J. Stokes Machine Co., of Philadelphia, Pa., which occupies comparatively little space and furnishes remarkably pure water in large quantities, varying from 5 to 100 gallons per hour, according to the size of the still.

In Fig. 225 is shown a sectional view of the automatic water still to give a better idea of its operation. The raw water or feed water, as it is generally termed, enters at "*H*," surrounds the condenser tubes "*C*," and serves to condense the steam generated in the still "*B*" as it descends in the condenser tubes, and in so doing becomes heated to the boiling point by the time it reaches the top, where the ammonia and other gases escape into the air through the opening "*E*." A part of this feed water escapes over the goose neck "*F*" either into a waste pipe overflow at "*G*," and the balance passes into the still through the passage "*M*." The still is operated by live

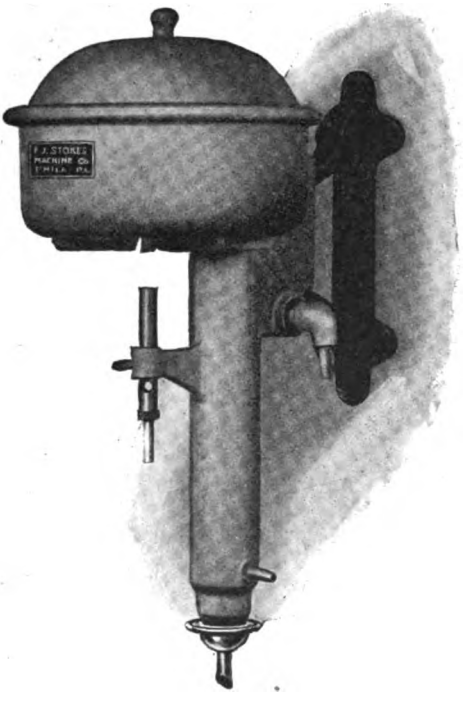


FIG. 226.

steam with a pressure of twenty pounds or more, which circulates in the copper coil "*D*." The distilled water comes out at "*J*," and can be piped to any receptacle. The condenser tubes extend to the extreme top of the steam chamber and high above the water level, so as to avoid the danger of water being carried over by the steam. All exposed parts of the still are tinned to prevent corrosion.

Smaller sizes of the Stokes automatic water still, slightly different in design (see Fig. 226), to be heated with gas, and having an hourly capacity of $\frac{1}{2}$ to $2\frac{3}{4}$ gallons of distilled water, are also made; these are well adapted to the needs of the retail pharmacist and smaller manufacturers.

CHAPTER XIV.

THE OFFICIAL SOLUTIONS OR LIQUORS.

THE term Liquor as used in the U. S. Pharmacopœia is generally applied to aqueous solutions of non-volatile substances. The exceptions are Liquor Ammonii Acetatis, completely volatilized by boiling; Liquor Formaldehydi, an aqueous solution of gaseous formaldehyde; Liquor Hydrogenii Dioxidi, completely volatilized by heat; Liquor Iodi Compositus, from which all the iodine can be volatilized by boiling, and much of it at even lower temperature. In Europe the term is indiscriminately applied to alcoholic, aqueous, and hydroalcoholic solutions of non-volatile and volatile inorganic and organic matter, and a similar condition exists in the case of the liquors of the *National Formulary*. Seventy-three liquors are recognized in the U. S. Pharmacopœia and the *National Formulary*, and of these 32 are made by simple solution of the medicinal agent in the solvent, while 41 involve chemical action in their preparation. The liquors may, therefore, be conveniently divided into two groups, as follows:

1. Simple Solutions.—The active ingredient is added directly to the water.

Latin name.	English name.	Composition.
Liquor Acidi Arsenosi U. S. P.	Solution of Arsenous Acid	An aqueous solution of arsenous and hydrochloric acids. Should contain an amount of arsenous acid corresponding to not less than 0.975 per cent., nor more than 1.025 per cent. of arsenic trioxide.
Liquor Antisepticus Nat. Form.	Antiseptic Solution	A hydroalcoholic solution of boric acid, thymol, eucalyptol, menthol, sodium salicylate, sodium benzoate, methyl salicylate and oil of thyme. Contains 30 per cent. of official alcohol, by volume.
Liquor Antisepticus Alkalinus Nat. Form.	Alkaline Antiseptic	A hydroalcoholic solution of potassium bicarbonate, sodium benzoate, sodium borate, thymol, eucalyptol, methyl salicylate, and oil of peppermint, colored red with cudbear. Contains 6 per cent. of alcohol and 15 per cent. of glycerin, by volume.
Liquor Arseni et Hydrargyri Iodidi U. S. P.	Solution of Arsenous and Mercuric Iodide (Donovan's Solution)	An aqueous solution of arsenous and red mercuric iodides.
Liquor Bismuthi Nat. Form.	Solution of Bismuth	A hydroalcoholic solution of bismuth and sodium tartrate. Contains 12½ per cent. of alcohol and 6¼ per cent. of glycerin, by volume.
Liquor Bromi Nat. Form.	Solution of Bromine (Smith's Solution of Bromine)	An aqueous solution of bromine and potassium bromide.

Latin name.	English name.	Composition.
Liquor Calcis . . . U. S. P.	Solution of Lime (Lime Water)	A saturated aqueous solution of calcium hydroxide. Contains about 0.17 per cent. at 15° C. (59° F.), but the percentage of calcium hydroxide decreases as the temperature rises.
Liquor Carmini . . Nat. Form.	Solution of Carmine . . .	An alkaline solution of carmine containing 36.5 per cent. by volume of glycerin.
Liquor Cocci . . . Nat. Form.	Cochineal Color	An aqueous solution of cochineal, made with the aid of potassium carbonate, alum and potassium bitartrate Contains about 3 per cent. of alcohol and 50 per cent. of glycerin, by volume.
Liquor Formaldehydi U. S. P.	Solution of Formaldehyde .	An aqueous solution of formaldehyde, containing not less than 37 per cent. of the gas.
Liquor Gutta-Perchæ Nat. Form.	Solution of Gutta-percha . .	A chloroform solution of gutta-percha, clarified by means of lead carbonate.
Liquor Hydrargyri et Potassii Iodidi . . Nat. Form.	Solution of Mercury and Potassium Iodide (Channing's Solution) . .	An aqueous solution of potassium and red mercuric iodides.
Liquor Hydrogenii Dioxidi . . . . U. S. P.	Solution of Hydrogen Dioxide (Solution of Hydrogen Peroxide	An acidulous aqueous solution containing not less than 3 per cent. by weight of hydrogen dioxide, corresponding to not less than 10 volumes of available oxygen.
Liquor Hydrastinæ Compositus . . Nat. Form.	Compound Solution of Hydrastine (Colorless Hydrastine Solution) . .	A solution of hydrastine hydrochloride and the chlorides of aluminum, calcium, magnesium, and potassium. Contains 50 per cent. by volume of glycerin.
Liquor Hypophosphitum . . . . . Nat. Form.	Solution of Hypophosphites .	An acidulated aqueous solution of calcium, potassium, and sodium hypophosphites.
Liquor Hypophosphitum Compositus . Nat. Form.	Compound Solution of Hypophosphites .	An aqueous solution of the hypophosphites of calcium, potassium, sodium, iron, manganese, quinine, and strychnine. Contains 25 per cent. by volume of glycerin and is flavored with orange flower water.
Liquor Hypophysis . U. S. P.	Solution of Hypophysis (Solution of the Pituitary Body) . . .	A solution containing the water-soluble principles from the fresh posterior lobe of the pituitary body of cattle.
Liquor Iodi Compositus . . . . . U. S. P.	Compound Solution of Iodine (Lugol's Solution) . . .	An aqueous solution of iodine and potassium iodide.
Liquor Pancreatini . Nat. Form.	Solution of Pancreatin (Pancreatic Solution)	A solution of pancreatin, sodium bicarbonate, sodium chloride, flavored with cardamom. Contains about 1.5 per cent. of alcohol, 0.2 per cent. of chloroform and 25 per cent. of glycerin, by volume.
Liquor Pepsini . . Nat. Form.	Liquid Pepsin .	An aqueous solution of pepsin and hydrochloric acid. Contains 34 per cent. by volume of glycerin.

Latin name.	English name.	Composition.
Liquor Pepsini Antisepticus . . . Nat. Form.	Antiseptic Solution of Pepsin	An aqueous solution of pepsin, menthol, eucalyptol and methyl salicylate. Contains about 1 per cent. of alcohol, 2 per cent. of diluted hydrochloric acid and 5 per cent. of glycerin, by volume.
Liquor Pepsini Aromaticus . . . . Nat. Form.	Aromatic Solution of Pepsin . .	An aqueous solution of pepsin and hydrochloric acid, flavored with the oils of cinnamon, clove, and pimenta. Contains 25 per cent. by volume of glycerin and also 3½ per cent. of alcohol.
Liquor Phosphori. . Nat. Form.	Solution of Phosphorus (Thompson's Solution of Phosphorus) .	An alcoholic solution of phosphorus, flavored with spirit of peppermint. Contains also 64½ per cent. by volume of glycerin.
Liquor Picis Alkalinus Nat. Form.	Alkaline Solution of Tar . .	An aqueous solution of tar and potassium hydroxide.
Liquor Picis Carbonis Nat. Form.	Coal Tar Solution	An alcoholic solution of coal tar made with the aid of soap bark.
Liquor Plumbi Subacetatis Dilutus . U. S. P.	Diluted Solution of Lead Subacetate (Lead Water) . .	A weak aqueous solution of lead subacetate, containing about 1 per cent. of the salt.
Liquor Potassii Hydroxidi . . . . U. S. P.	Solution of Potassium Hydroxide . .	A 5 per cent. (not less than 4.5 per cent.) aqueous solution of potassium hydroxide.
Liquor Sodæ et Menthæ . . . . . Nat. Form.	Solution of Soda and Mint (Soda Mint) . . .	A solution of sodium bicarbonate in spearmint water, and containing 1 per cent. of aromatic spirit of ammonia.
Liquor Sodii Arsenatis U. S. P.	Solution of Sodium Arsenate . .	A 1 per cent. aqueous solution of anhydrous sodium arsenate.
Liquor Sodii Arsenatis (Pearson) . . . Nat. Form.	Pearson's Solution of Sodium Arsenate . . .	A $\frac{1}{10}$ per cent. aqueous solution of anhydrous sodium arsenate.
Liquor Sodii Boratis Compositus . . Nat. Form.	Compound Solution of Sodium Borate (Dobell's Solution) . .	An aqueous solution of sodium borate, sodium bicarbonate, and phenol. Contains 3½ per cent. by volume of glycerin.
Liquor Sodii Chloridi Physiologicus . . U. S. P.	Physiological Solution of Sodium Chloride (Physiological Salt Solution, Normal Salt Solution) . . .	An aqueous solution of sodium chloride, containing 8.5 Gms. of the salt in 1000 mils. (or Cc.).
Liquor Sodii Glycerophosphatis . . . U. S. P.	Solution of Sodium Glycerophosphate .	An aqueous solution of sodium glycerophosphate, containing not less than 50 per cent. of the anhydrous salt.
Liquor Sodii Hydroxidi . . . . . U. S. P.	Solution of Sodium Hydroxide .	A 5 per cent. aqueous solution of sodium hydroxide.
Liquor Zinci et Aluminis Compositus . Nat. Form.	Compound Solution of Zinc and Aluminum .	An aqueous solution of aluminum and zinc sulphates, beta-naphthol, and oil of thyme.
Liquor Zinci et Ferri Compositus . . Nat. Form.	Compound Solution of Zinc and Iron (Deodorant Solution) . .	An aqueous solution of iron, copper and zinc sulphates, beta-naphthol, and oil of thyme.

2. Chemical Solutions.—The active ingredient is formed in the process of manufacture, as the result of chemical action.

Latin name.	English name.	Process of manufacture.
Liquor Alumini Acetatis (Liquor Burowii). . . . . Nat Form.	Solution of Aluminum Acetate Burow's Solution . . .	An aqueous solution of normal aluminum acetate, made by mutual decomposition of solutions of aluminum sulphate and lead acetate and straining the mixture. Contains about 0.05 Gm. of aluminum acetate in each mil. (or Cc.).
Liquor Alumini Acetico-Tartratis . . Nat. Form.	Solution of Aluminum Acetico-Tartrate . .	Made by dissolving freshly precipitated aluminum hydroxide in water with the aid of tartaric and glacial acetic acids. Contains about 50 per cent. of the aluminum compound.
Liquor Alumini Subacetatis . . . . . Nat. Form.	Solution of Aluminum Subacetate . . .	Made by decomposing a solution of aluminum sulphate with calcium carbonate and acetic acid. Contains about 7.5 per cent. of basic aluminum acetate, $Al(C_2H_3O_2)_2OH$.
Liquor Ammonii Acetatis . . . . . U. S. P.	Solution of Ammonium Acetate (Spirit of Mindererus) . .	Made by dissolving ammonium carbonate in diluted acetic acid. Contains about 7 per cent. of ammonium acetate.
Liquor Ammonii Citratis . . . . . Nat. Form.	Solution of Ammonium Citrate	Made by neutralizing an aqueous solution of citric acid with ammonia water.
Liquor Arsenicalis, Clemens . . . Nat. Form.	Clemens' Solution of Arsenic (Solution of Potassium Arsenate and Bromides) . .	Made by dissolving arsenic trioxide and potassium bicarbonate in water with the aid of heat, and when cool, adding bromine. Contains arsenic in combination corresponding to about 1 per cent. of arsenic trioxide.
Liquor Auri et Arseni Bromidi . . . Nat. Form.	Solution of Gold and Arsenic Bromide . .	Made by dissolving arsenic trioxide and bromine in water with the aid of a gentle heat, expelling the excess of bromine and finally dissolving bromauric acid in the solution.
Liquor Calcis Sulphuratæ . . . . . Nat. Form.	Solution of Sulphurated Lime (Vleminck's Solution, Vleminck's Lotion)	Made by boiling a mixture of slaked lime and sulphur with water and straining the liquid.
Liquor Chlori Compositus . . . . . Nat. Form.	Compound Solution of Chlorine	Made by heating a mixture of potassium chlorate, hydrochloric acid, and water for a few minutes on a waterbath, and then adding two or three successive portions of water. Contains, when freshly prepared, about 0.35 per cent. of chlorine, together with some oxides of chlorine and potassium chloride.
Liquor Cresolis Compositus . . . . . U. S. P.	Compound Solution of Cresol	Made by incorporating a solution of soft soap, prepared from linseed oil, potassium hydroxide, alcohol, and water, with the aid of heat, with an equal weight of cresol, and stirring until a clear solution results.

Latin name.	English name.	Process of manufacture.
Liquor Ferri Acetatis Nat. Form.	Solution of Ferric Acetate	Made by dissolving freshly prepared ferric hydroxide in water with the aid of glacial acetic acid. Contains about 31 per cent. of anhydrous ferric acetate.
Liquor Ferri Albuminati Nat. Form.	Solution of albuminate of Iron	Made by adding a solution of ferric oxychloride to a solution of fresh egg albumen in water; after 2 hours solution is effected by means of sodium citrate and finally alcohol, aromatic elixir and water are added. Contains about 22 per cent. by volume of alcohol.
Liquor Ferri Chloridi U. S. P.	Solution of Ferric Chloride	Made from iron wire, hydrochloric acid, and water, with the aid of nitric acid. Should contain an amount of ferric chloride corresponding to not less than 10 per cent. of metallic iron.
Liquor Ferri Citratis Nat. Form.	Solution of Ferric Citrate	Made by dissolving freshly prepared ferric hydroxide in water with the aid of citric acid. Contains an amount of ferric citrate corresponding to not less than 7.25 per cent. of metallic iron.
Liquor Ferri et Ammonii Acetatis U. S. P.	Solution of Iron and Ammonium Acetate (Basham's Mixture)	Made by mixing solution of ammonium acetate, diluted acetic acid, and tincture of ferric chloride; then adding aromatic elixir, glycerin, and water.
Liquor Ferri Hypophosphitis Nat. Form.	Solution of Ferric Hypophosphite	Made by dissolving freshly precipitated ferric hypophosphite in water with the aid of potassium citrate. Contains 15 per cent. by volume of glycerin.
Liquor Ferri Nitratis Nat. Form.	Solution of Ferric Nitrate	Made by dissolving freshly prepared ferric hydroxide in water with the aid of nitric acid. Contains an amount of ferric nitrate corresponding to not less than 1.3 per cent. of metallic iron.
Liquor Ferri Oxychloridi Nat. Form.	Solution of Ferric Oxychloride	Made by dissolving freshly prepared ferric hydroxide in water with the aid of a small quantity of hydrochloric acid (insufficient to form the normal chloride); after standing for 3 days, the mixture is heated to 40° C. (104° F.) to facilitate solution. The finished product contains 12.5 per cent. by volume of glycerin.
Liquor Ferri Oxysulphatis Nat. Form.	Solution of Oxysulphate of Iron	Made by adding nitric acid to a boiling solution of ferrous sulphate and continuing the application of heat.

Latin name.	English name.	Process of manufacture.
Liquor Ferri Peptonati . . . . . Nat. Form.	Solution of Peptonate of Iron	Made by adding solution of ferric oxychloride and sodium citrate to a freshly prepared and previously neutralized solution of peptone (made from egg albumen); when perfect solution has been effected, an alcoholic solution of oil of orange, vanillin and acetic ether is added as flavoring, and finally syrup and glycerin and sufficient water to make up the required volume. Contains 15 per cent. by volume of alcohol, and 5 per cent. each of syrup and glycerin.
Liquor Ferri Peptonati et Mangani . Nat. Form.	Solution of Peptonate of Iron and Manganese	This solution is made exactly like the preceding preparation, except that an addition of soluble manganese citrate is made.
Liquor Ferri Protochloridi . . . . Nat. Form.	Solution of Ferrous Chloride	Made by dissolving iron wire in hydrochloric acid and water with the aid of heat, and adding glycerin and diluted hypophosphorous acid as a preservative.
Liquor Ferri Salicylatis . . . . . Nat. Form.	Solution of Ferric Salicylate (Salicylated Mixture of Iron . .	Made by adding tincture of citrochloride of iron to a solution of ammonium citrate and sodium salicylate. Contains 17.5 per cent. by volume of glycerin and is flavored with methyl salicylate.
Liquor Ferri Subsulphatis . . . . U. S. P.	Solution of Ferric Subsulphate (Monsel's Solution) . . .	Made by adding ferrous sulphate to a heated mixture of sulphuric and nitric acids and water. Contains basic ferric sulphate corresponding to not less than 13.57 per cent. of metallic iron.
Liquor Ferri Tersulphatis . . . . U. S. P.	Solution of Ferric Sulphate . .	Made like the preceding solution, except that a larger proportion of sulphuric acid is used. Should contain an amount of normal ferric sulphate corresponding to not less than 10 per cent. of metallic iron.
Liquor Hydrargyri Nitratis . . . . Nat. Form.	Solution of Mercuric Nitrate .	Made by dissolving red oxide of mercury in a mixture of nitric acid and water. Contains about 60 per cent. of murcuric nitrate and about 11 per cent. of free nitric acid.
Liquor Iodi Phenolatus (Liquor Iodi Carbolatus) . . . . Nat. Form.	Phenolated Solution of Iodine (Carbolized Solution of Iodine, Boulton's Solution . . .	Made by mixing liquefied phenol with compound solution of iodine, and adding glycerin and water.
Liquor Magnesii Citratis . . . . . U. S. P.	Solution of Magnesium Citrate	Made by dissolving magnesium carbonate in a solution of citric acid; then adding syrup of citric acid and water, and finally potassium or sodium bicarbonate. Should contain an amount of magnesium citrate corresponding to not less than 1.5 Gms. of magnesium oxide in 100 mils. (or Cc.).

Latin name.	English name.	Process of manufacture.
Liquor Magnesii Sulphatis Effervescens Nat. Form.	Effervescent Solution of Magnesium Sulphate	Made by adding citric acid and syrup of citric acid to a solution of magnesium sulphate in water; finally adding potassium bicarbonate.
Liquor Phosphatum Acidus Nat. Form.	Solution of Acid Phosphates	Made by dissolving precipitated calcium carbonate and magnesium carbonate in a mixture of phosphoric acid and water.
Liquor Phosphatum Compositus Nat. Form.	Compound Solution of Phosphates	Made by dissolving precipitated calcium carbonate, potassium bicarbonate and sodium bicarbonate in a mixture of citric acid, glycerin and orange flower water, gradually adding phosphoric acid; to this solution is added an aqueous solution of ammonium phosphate and ferric phosphate. Contains 37.5 per cent. by volume of glycerin.
Liquor Plumbi Subacetatis U. S. P.	Solution of Lead Subacetate (Goulard's Extract)	Made by boiling lead oxide with a solution of lead acetate. Should contain an amount of lead subacetate corresponding to not less than 18 per cent., of metallic lead.
Liquor Potassii Arsenitis U. S. P.	Solution of Potassium Arsenite (Fowler's Solution)	Made by dissolving arsenic trioxide and potassium bicarbonate in boiling water and adding compound tincture of lavender. Should contain an amount of potassium arsenite corresponding to not less than 0.975 per cent. nor more than 1.025 per cent. of arsenic trioxide.
Liquor Potassii Citratis U. S. P.	Solution of Potassium Citrate (Neutral Mixture)	Always freshly made by mixing a solution of potassium bicarbonate with one of citric acid, and containing not less than 8 per cent. of potassium citrate.
Liquor Potassæ Chlorinatæ Nat. Form.	Solution of Chlorinated Potassa (Javelle Water)	Made by pouring a hot solution of potassium carbonate into a mixture of chlorinated lime and water, and when cool, straining the mixture.
Liquor Sodæ Chlorinatæ U. S. P.	Solution of Chlorinated Soda (Labarraque's Solution)	Made by adding a hot solution of sodium carbonate to a solution of chlorinated lime. The chlorine compounds of sodium present should contain at least 2.5 per cent. of available chlorine.
Liquor Sodii Citratis Nat. Form.	Solution of Sodium Citrate (Potio Riveri)	Made by adding sodium bicarbonate to an aqueous solution of citric acid.
Liquor Sodii Citro-Tartratis Effervescens Nat. Form.	Effervescent Solution of Sodium Citro-Tartrate (Tartro-Citric Lemonade)	Made by dissolving sodium bicarbonate in a solution of citric and tartaric acids; then adding syrup of citric acid and water. and finally sodium bicarbonate.

Latin name.	English name.	Method of Preparation.
Liquor Sodii Phosphatis Compositus . . Nat. Form.	Compound Solution of Sodium Phosphate .	Made by heating a mixture of uneffloresced sodium phosphate and citric acid until liquefied; after filtering the hot liquid, glycerin is added and sufficient distilled water, previously boiled, to make up the required quantity of solution. Contains 1 Gm. of sodium phosphate in each mil. (or Cc.) of the solution, and 15 per cent. by volume of glycerin.
Liquor Strychninæ Acetatis . . . . Nat. Form.	Solution of Strychnine Acetate (Hall's Solution of Strychnine)	Made by dissolving strychnine in diluted acetic acid and adding alcohol, compound tincture of cardamom and water. Contains 0.00178 Gm. of strychnine in each mil. (or Cc.) of the solution, and 25 per cent. by volume of alcohol.
Liquor Zinci Chloridi U. S. P.	Solution of Zinc Chloride . .	Made by dissolving granulated zinc in hydrochloric acid and water, and freeing the solution from iron by means of nitric acid and zinc carbonate.

CHAPTER XV.

DECOCTIONS AND INFUSIONS.

DECOCTIONS.

DECOCTIONS are aqueous solutions of the ative principles of vegetable drugs, prepared at a boiling temperature. This process is obviously not adapted to drugs containing volatile principles, nor to those whose activity depends upon resinous constituents. Drugs of a very close texture, or the active virtues of which cannot be exhausted below the temperature of boiling water, are best suited for the process of decoction. In former years decoctions were extensively employed, and frequently made by using a large quantity of water and boiling it down, in open vessels, to one-half, or even to a less amount. This method offered no obvious advantage, and, in fact, often proved decidedly disadvantageous on account of the deleterious effect upon the constituents of the drug from long exposure to air and heat. In this country, at least, decoctions have almost entirely disappeared from the physician's armamentarium, and the pharmacist is but rarely called upon to prepare them.

Decoctions as well as infusions must always be prepared extemporaneously, since they will readily deteriorate on account of the perishable matter in solution and the absence of alcohol or other preservative.

The Pharmacopœia gives the following general directions for preparing decoctions whenever a special strength is not indicated by the physician: Put 50 Gms. of the substance, coarsely communited, into a suitable vessel provided with a cover; pour upon it 1000 mils. (or Cc.) of cold water, cover well, and boil for fifteen minutes; then let it cool to about 40° C. (104° F.) express, strain the expressed liquid, and pass through the strainer enough cold water to make the product measure 1000 mils. (or Cc.).

The use of cold water, to begin with, insures the complete extraction from the drug of all its soluble principles, by the gradually heated water, the albuminous matter being subsequently coagulated as the heat is increased to near the boiling point. If, on the other hand, the drug be at once immersed in boiling water, the albumen contained in cells would be coagulated and thus seriously interfere with the extraction of the other constituents. In preparing compound decoctions, all the drugs may be added to the cold water, with the exception of those which, like senna, are injured by long-continued heat, or which contain aromatic or other volatile principles; such should be added

when the decoction is ready to be removed from the fire or steambath and allowed to digest until it is sufficiently cooled for straining. The material should in all cases be cut or bruised, the degree of fineness depending upon the nature of the tissue. Woody drugs may be reduced to a moderately fine powder; leaves, however, and other drugs consisting mainly of loose parenchyma, are better used in the form of a moderately coarse or very coarse powder.

Unless the liquid is to be considerably boiled down, decoctions are best prepared in a vessel provided with a cover, which may be loosely put on until the boiling is completed, when the vessel should be well closed, particularly if additions have been made at the close of boiling. Porcelain is undoubtedly the best material for vessels used for preparing decoctions, since it is not acted upon by the various vegetable principles; for similar reasons, glass flasks will answer a useful purpose in making small quantities of these preparations. As a rule, it is best to avoid metallic vessels, except when made of block tin and used in connection with a steambath. As many drugs contain tannin, vessels made of iron are not adapted for preparing their decoctions, and the usually imperfect covering of galvanized or tinned sheet iron renders vessels lined with such material but little better suited for this purpose, and still inferior to properly enamelled iron vessels.

As a rule, decoctions should be allowed to cool below 40° C. (104° F.) before they are strained; principles which are soluble only in hot water are then mostly precipitated, and removed without, in most cases, weakening the medicinal value of the preparations; but, even with this precaution, the strained liquid may become unsightly in appearance through the further deposition, on cooling, of apotheme or matter soluble only in hot water. In such cases the pharmacist should be guided by the directions of the Pharmacopœia or the intentions of the physician, and not sacrifice effect to elegance.

The *National Formulary* recognizes one decoction, namely, Compound Decoction of Sarsaparilla, which is made by boiling a mixture of sarsaparilla and guaiacum wood with water, in a covered vessel, for thirty minutes, then adding sassafras, glycyrrhiza and mezereum and macerating the mixture for two hours. It is finally strained and cold water added to make up the required volume.

In the British Pharmacopœia, 7 decoctions are recognized, all of which are directed to be made with distilled water, and in the majority of the formulas boiling is directed to be continued for only ten minutes.

The German Pharmacopœia directs decoctions to be made of the strength of 10 per cent. when not otherwise specified, by adding the drug to cold water and keeping the mixture for half an hour in a bath of steam arising from boiling water, and then expressing while warm. Two preparations termed *decoctions*, of althæa and of flaxseed, are prepared cold by maceration for half an hour and subsequent gentle expression; they belong more properly under the head of *mucilages*.

INFUSIONS.

Infusions are aqueous solutions of the soluble principles of vegetable or animal drugs, obtained by maceration or digestion in hot or cold water, and differ from decoctions only in the lower degree of heat employed in their preparation. This process is particularly suitable for substances containing volatile or other principles which would be dissipated or injured by boiling. A convenient apparatus, well adapted for making these preparations, is Squire's infusion pot, Fig. 227. This consists of the jar, *A*, with a projecting ledge near the top, which supports a strainer, *B* or *D*, containing the material to be exhausted; the jar is closed by a well fitting cover, *C*. The advantages of this contrivance are that the material is exhausted by circulatory displacement—the liquid, as it becomes charged with the soluble ingredients, descending to the bottom, giving place to fresh portions of less saturated menstruum—and that no further straining will be required if care has been taken to use not too fine a powder.

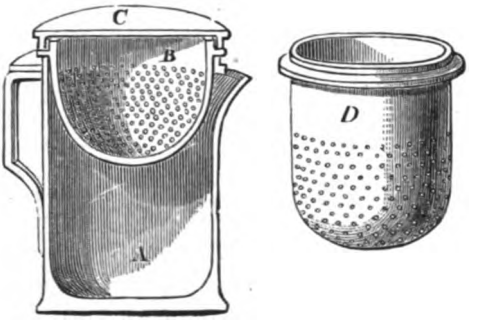


FIG. 227.—Squire's infusion pot.

Drugs are best adapted for exhaustion with water when cut into thin slices by means of a suitable knife, so that they may easily be permeated by the liquid; if cutting be inadmissible, they should be bruised to a coarse powder. Ligneous drugs, however, should be in a fine or moderately fine powder, which is best adapted also for most of those infusions which may be made by percolation.

Wherever possible infusions should be made in porcelain or porcelain-lined vessels, to avoid contact with metal.

The U. S. Pharmacopœia has adopted the plan of ordering all infusions, unless otherwise directed by the physician, with the exception of two specially enumerated, to be made of 1 part of material to 20 parts of infusion, according to the following directions: Infusions must be *freshly made from the drug*, and, when the strength is not directed by the physician nor specified by the Pharmacopœia, shall be prepared by the following formula: Take of the substance, coarsely comminuted, 50 Gms.; boiling water, 1000 mils. (or Cc.); water, a

sufficient quantity to make 1000 mils. (or C.c.). Put the substance into a suitable vessel provided with a cover, pour upon it the boiling water, cover the vessel tightly, and let it stand for one-half hour in a warm place. Then strain with expression, and pass sufficient water through the strainer to make the infusion measure 1000 mils. (or Cc.).

Both in the cases of decoctions and infusions the Pharmacopœia requires that, when made of energetic or powerful substances, the physician shall specify the desired strength.

Two infusions are recognized in the Pharmacopœia, both being prepared by maceration with hot water; the time directed for the latter method is specified.

The *National Formulary* recognizes five infusions, of which two are made by hot infusion and three by cold percolation.

The strength of infusions of the German Pharmacopœia is double that of our own, but the general directions given for their preparation are nearly identical with the above, from which they differ only in that the mixture of drug and boiling water is heated for five minutes in a vapor bath of boiling water, occasionally stirred, allowed to cool, and strained.

INFUSIONS OF THE PHARMACOPŒIA AND NATIONAL FORMULARY.

MADE BY HOT MACERATION.

Latin name.	English name.	Method of preparation.
Infusum Brayeræ. Nat. Form.	Infusion of Brayera, Infusion of Cousso	Made by pouring boiling water over coarsely powdered brayera and macerating until cool. This infusion is dispensed without straining.
Infusum Digitalis U. S. P	Infusion of Digitalis	Upon 15 Gms. of digitalis pour 500 mils. (or Cc.) of boiling water and let it macerate in a covered vessel for 1 hour. Then strain and to the liquid add 150 mils. (or Cc.) of cinnamon water, and pass enough cold water through the residue to make the liquid measure 1000 mils. (or Cc.).
Infusum Rosæ Compositum Nat. Form	Compound Infusion of Rose	Made by pouring boiling water on red rose in a porcelain vessel, adding diluted sulphuric acid, and digesting for an hour; after straining, sugar is dissolved in the liquid.
Infusum Sennæ Compositum U. S. P.	Compound Infusion of Senna	Pour 800 mils. (or Cc.) of boiling water upon 60 Gms. of senna, 120 Gms. of manna, and 20 Gms. of bruised fennel and macerate in a covered vessel for half an hour. Express, and in the strained infusion dissolve 120 Gms. of magnesium sulphate. Again strain and pass enough cold water through the first residue to make the liquid measure 1000 mils. (or Cc.).

MADE BY PERCOLATION.

Latin name.	English name.	Method of preparation.
Infusion Cinchonæ Nat. Form.	Infusion of Cinchona	Made by percolating ground cinchona with a mixture of aromatic sulphuric acid and water.
Infusum Gentianæ Compositum Nat. Form.	Compound Infusion of Gentian	Made by percolating a mixture of gentian, coriander, and bitter orange peel with diluted alcohol, the tincture being subsequently mixed with 3 times its volume of water.
Infusum Pruni Virginianæ Nat. Form.	Infusion of Wild Cherry	Made by macerating ground wild cherry bark with water for 3 hours, then percolating and adding glycerin to the percolate.

Infusions are evidently in greater favor with medical men in Great Britain than elsewhere, as the last edition of the British Pharmacopœia gives directions for the preparation of 20 infusions. The time allowed for maceration varies from 15 minutes to 1 hour, the mixture being strained while hot.

CHAPTER XVI.

SYRUPS.

In pharmacy the term syrup is applied to concentrated solutions of sugar, the solvent being either water or an aqueous, acetous, or hydro-alcoholic solution of some medicinal or aromatic principle. The Pharmacopœia applies the name *syrupus* or *syrup* to a nearly saturated solution of sugar in water; in practice this solution is usually termed *simple syrup* as a mark of distinction. Syrups are an old and favorite form of administering medicines, partly on account of the sweet taste, and partly because sugar is used as a preservative for otherwise unstable vegetable solutions, in place of alcohol, which is often contraindicated in disease. The sugar used in making syrups should be of the best quality obtainable, as upon it depends the character and stability of the finished syrup. The Pharmacopœia describes sugar as occurring in white, hard, crystalline granules, of purely sweet taste, which corresponds to the best commercial varieties known as granulated and cut-loaf sugar; in order to overcome the yellowish cast of sugar, refiners sometimes add ultramarine, Prussian blue, etc., which will pass to some extent even through paper filters and finally deposit in the syrup containers. The variety of sugar known in commerce as "Crystal Sugar A" is undoubtedly the best for pharmaceutical purposes.

Sugar is soluble in half its weight of water at 15° C. (59° F.), and a saturated solution thus prepared has the specific gravity of 1.345; it is also soluble in 175 times its weight of official alcohol. Large quantities of sugar dissolved in water very materially increase the bulk of the liquid, a fact which must always be borne in mind in the preparation of syrups; practically, two-thirds of the weight of sugar will equal its bulk in fluid measure, or, in other words, 750 Gms. of sugar when dissolved in water will increase the bulk of the liquid by nearly 500 mils. (or Cc.). The proper proportion of sugar to menstruum is of great importance, as upon it depends the stability of the syrup. Should the sugar be deficient in quantity, it will not efficiently protect the other organic principles in the syrup, and the latter would be liable to ferment. On the other hand, if too much sugar be dissolved by the aid of heat, the excess will crystallize out after cooling. If alcohol be present in the menstruum, less sugar will be taken up by the liquid than in the case of pure water as shown by the following table, but at the same time less sugar is required to insure stability owing to the preservative properties of the alcohol.

SOLUBILITY OF CANE SUGAR IN MIXTURES OF ALCOHOL AND WATER.
(According to Schufeldt.)

Percentage of alcohol in the mixture. By volume.	By weight.	Percentage of sugar in solution.	Number of Grams of sugar soluble in 100 Cc. of the mixture.
0.	0	66.20	195.8
6.	5	64.25	179.7
12.	10	62.20	164.5
18.	15	60.40	152.5
24.	20	58.55	141.2
30.	25	56.20	128.3
36.	30	54.05	117.8
42.	35	51.25	105.3
47.	40	47.75	91.3
58.5	50	38.55	62.7
67.5	60	26.70	36.4
77.	70	12.25	13.9
85.5	80	4.05	4.2
93.5	90	0.95	0.09
96.75	95	0.15	0.01

Preparation.—In the preparation of syrups, solution of the sugar may be effected by one of the following methods: Agitation of sugar and solvent without heat, cold percolation of the sugar with the solvent, gentle heating of the sugar and solvent, or heating the mixture of sugar and solvent to the boiling point. The application of heat in the manufacture of syrups should be avoided as far as possible, especially a boiling temperature, partly to prevent the loss of volatile constituents and partly to guard against any change in the character of the sugar, which, under the influence of heat and particularly with acid liquids, is converted into inverted sugar, resembling glucose, and thereby predisposed to fermentation; moreover, the use of heat in open vessels causes evaporation of a part of the solvent, which, if not restored, produces a supersaturated solution with the attending evil of crystallization referred to above.

The preparation of syrups without heat is a feature of American pharmacy, both the British and German Pharmacopœias directing the use of heat in every instance. By some authorities it is claimed that syrups made with heat are more permanent than those made cold; this claim is not supported by experience in this country. For all syrups containing volatile principles or such as may be changed by heat, the cold process is decidedly preferable, and if pure sugar be used, such syrups keep admirably.

The process of cold percolation of sugar with the solvent was first suggested by L. Orinsky in 1871, and is now largely recommended in the Pharmacopœia; the process is of decided advantage whenever the syrup is to be prepared without heat, although it requires a little care in its management so as to insure perfect solution and a clear percolate. A cylindrical, slightly tapering percolator is best adapted for the purpose. A clean, soft piece of sponge is placed, with moderate pressure, in the neck of the percolator (if too tightly compressed, the viscid liquid will not pass through; and if too loose, the liquid passes

too rapidly and not clear); upon it is poured the sugar in granular form, and properly levelled and shaken down by tapping the sides of the percolator, after which a diaphragm of filter paper is laid on the surface and the solvent carefully poured on with the aid of a guiding rod. If the sponge or a tuft of absorbent cotton has been properly adjusted, the solution will be perfectly clear and transparent, and pass out in drops only, all the sugar being taken up before the end of the process; but if the liquid passes too rapidly, or if it be turbid, it must be poured back into the percolator until the defect is remedied. It will be found advantageous to close the lower orifice of the percolator with a sound cork (or if a rubber tube be used, to tie the same up on the side of the percolator) as soon as the menstruum reaches the sponge or cotton, and allow it to remain closed for a short while, possibly an hour or two, so that the menstruum may have an opportunity of becoming saturated, and thus a more gradual and more satisfactory flow of the percolate be established. Some objections have been made to this process, such as the time necessary for perfect solution of the sugar, and the fact that albuminous principles liable to induce fermentation are best removed by heat; but it must be borne in mind that cold percolation requires very little attention after it has once been started, can be allowed to go on during the night, and does away with the necessity of subsequant filtration; the evil tendency of nitrogenized principles in the solvent may be overcome by the use of weak alcohol and glycerin, as is directed in many of the official formulas.

In the case of some syrups, where the viscid character of the solvent precludes rapid solution of the sugar, or when the syrup is wanted in a hurry, a moderate heat may be employed to facilitate solution, by putting the sugar and solvent into a strong bottle one and a half times as large as the required volume of syrup, and, after securely corking, keeping it in a waterbath at a temperature of about 50° C. (122° F.), and frequently agitating until perfect solution is effected; all loss of volatile principles is avoided by keeping the bottle well corked. Whenever the solvent contains latent ferments or a large proportion of albuminous matter, heating to the boiling point is necessary, in order to render such principles harmless, as in the case of syrups prepared from fruit juices; but the heat should not be continued beyond the boiling point, to avoid a change in the sugar.

When large quantities of syrup are to be made with heat, the mixture of sugar and solvent is placed in a porcelain-lined or well tinned kettle and heated over a direct fire or on a steambath until the sugar is dissolved; it is then strained and water added to make up the desired volume.

The appearance of colorless or slightly colored syrups will be materially improved if they are filtered through paper; this treatment, which also adds to the keeping quality of the syrups, must always be conducted in well covered funnels to prevent evaporation of the solvent.

Fruit syrups are no longer recognized in the U. S. Pharmacopœia. They are usually prepared by crushing the fruit and setting it aside at a moderate temperature, 20° to 25° C. (68°–77° F.), for several days, for the purpose of destroying certain undesirable principles known as pectin or vegetable jelly, which, if allowed to remain in the fruit juice, are apt to cause the syrup to gelatinize. The complete removal of pectin is determined by means of alcohol, which should mix clear with twice its volume of the fruit juice; a concentrated solution of mangesium sulphate should also leave the filtered juice unaffected.

The fermentation of fruit juices is usually conducted in casks or containers tightly closed, but provided with a suitable means of escape for the carbon dioxide gas generated during the process, which latter is allowed to pass by means of a glass tube through water contained in a small bottle; the end of the fermentative process is indicated when gas bubbles cease to escape through the water. Experience has shown that the addition of a small quantity of sugar (2 per cent. of the weight of the fruit) hastens fermentation, preserves the color, and facilitates subsequent filtration of the juice.

After removal of the pectin the pulp is expressed and the juice allowed to subside in well closed vessels, in a cool place, for two or three days until clear; the supernatant liquid must be carefully decanted or withdrawn and passed through a previously wetted paper filter. Sugar to the extent of 6 pounds to every 4 pounds of filtered juice should be added to the filtrate without delay and dissolved by stirring before the mixture is heated to boiling; any albuminous matter remaining in the juice is coagulated by heating and removed by subsequent straining. The mixture of filtered juice and sugar must not be boiled for any length of time, but the heat should be withdrawn when the syrup begins to boil quietly after the first frothing and rising of the liquid.

This process is applicable alike to the syrups of blackberries, cherries, raspberries, and strawberries.

Preservation.—Syrups are best preserved in completely filled bottles, in a cool place, and will keep unaltered for a long time if properly prepared; the addition of preservatives, such as salicylic or boric acid, calcium sulphite, ether, etc., is unnecessary, and, in fact, objectionable, and such syrups as cannot be kept with ordinary care should be made in small quantity only. It is well known that syrups containing acids gradually show a change in the sugar from cane sugar to inverted sugar, and it has been shown in an interesting series of experiments with the official syrups, by Woltersdorf and Richtmann, 1900, that the inversion is in direct proportion to the temperature to which the syrup is exposed; also that mineral acids cause greater inversion than organic acids, and that the presence of neutral salts in the syrup has the tendency to retard the inverting action of the acid. Air and heat are far more detrimental to the stability of sugar solutions than diffused light; but direct sunlight should always be avoided on account of the

heat transmitted by the sun's rays. When syrups have undergone fermentation they are no longer fit for use, and even if the attempt be made to restore them by boiling, they are likely soon to spoil again, owing to the decreased proportion of sugar left in solution; the best and safest plan is to throw them away. Finished syrups should always be put into perfectly *clean and dry* bottles (if made by heat, not until they have become cold), so as to avoid dilution and possible contamination with fermentation germs, which are likely to lurk in imperfectly cleaned bottles. Bottles from which syrups have been dispensed should be thoroughly washed with weak lye and afterward with water, and then dried before they are refilled.

All syrups, whether made by cold or hot process (except cold percolation), require straining through flannel previously moistened and expressed to remove particles of dust and dirt; and in the case of colorless or light-colored syrups, their appearance will be greatly improved by filtering them, under cover, through paper or a pledget of cotton.

ALPHABETICAL LIST OF U. S. P. SYRUPS.

Latin name.	English name.	Method of preparation.
Syrupus	Syrup	Made by dissolving sugar in distilled water by means of percolation or with the aid of heat.
Syrupus Acaciæ	Syrup of Acacia	Made by dissolving selected acacia in cold distilled water, and then dissolving sugar in the mucilage with the aid of heat.
Syrupus Acidi Citrici	Syrup of Citric Acid	Made by dissolving citric acid in distilled water, and then adding syrup and tincture of fresh lemon peel.
Syrupus Acidi Hydriodici	Syrup of Hydriodic Acid	Made by mixing diluted hydriodic acid, distilled water, and syrup. Contains about 1.38 Gms. of absolute hydriodic acid in 100 mils. (or Cc.).
Syrup Aurantii	Syrup of Orange	Made by triturating tincture of sweet orange peel with purified talc and distilled water, filtering the mixture, and dissolving citric acid and sugar in the filtrate by agitation.
Syrupus Aurantii Florum	Syrup of Orange Flowers	Made by dissolving sugar in orange flower water by agitation or by percolation.
Syrupus Calcii Lactophosphatis	Syrup of Calcium Lactophosphate	Made by dissolving calcium carbonate in lactic acid and distilled water, adding phosphoric acid and water to the solution, filtering, adding orange flower water and glycerin, and dissolving sugar in the liquid by agitation.
Syrupus Ferri Iodidi	Syrup of Ferrous Iodide	Made by preparing a solution of ferrous iodide from iodine, iron wire, and distilled water, heating to boiling and adding sugar; then filtering and dissolving sugar in the filtrate with the aid of heat; lastly adding diluted hypophosphorous acid and distilled water.

Latin name.	English name.	Method of Preparation.
Syrupus Hypophosphitum	Syrup of Hypophosphites	Made by adding diluted hypophosphorous acid to an aqueous solution of the hypophosphites of calcium, sodium, and potassium; filtering, adding glycerin and dissolving sugar in the filtrate by agitation.
Syrupus Ipecacuanhæ	Syrup of Ipecac	Made by mixing fluidextract of ipecac with acetic acid and water, shaking and filtering after 24 hours; to the filtrate add glycerin and dissolve sugar therein by agitation.
Syrupus Lactucarii	Syrup of Lactucarium	Made by dissolving citric acid in orange flower water, adding tincture of lactucarium and glycerin, and finally sufficient syrup to make up the required volume.
Syrupus Picis Liquidæ	Syrup of Tar	Made by dissolving tar in alcohol, adding magnesium carbonate, sugar, and water, and filtering the mixture after 2 hours; finally dissolving sugar in the filtrate by agitation or percolation.
Syrupus Pruni Virginianæ	Syrup of Wild Cherry	Made by macerating wild cherry bark with a mixture of glycerin and water for 24 hours, then percolating with water, and dissolving sugar in the liquid by agitation.
Syrupus Rhei	Syrup of Rhubarb	Made by mixing fluidextract of rhubarb and spirit of cinnamon with a solution of potassium carbonate, and then adding sufficient syrup to make up the required volume.
Syrupus Rhei Aromaticus	Aromatic Syrup of Rhubarb (Spiced Syrup of Rhubarb)	Made by dissolving potassium carbonate in aromatic tincture of rhubarb and adding sufficient syrup to make up the required volume.
Syrupus Sarsaparillæ Compositus	Compound Syrup of Sarsaparilla	Made by mixing fluidextracts of sarsaparilla, licorice, and senna with an alcoholic solution of methyl salicylate, oil of anise and oil of sassafras, and adding sufficient syrup to make up the required volume.
Syrupus Scillæ	Syrup of Squill	Made by dissolving sugar in vinegar of squill and then adding sufficient water to make up the required volume.
Syrupus Scillæ Compositus	Compound Syrup of Squill	Made by mixing an aqueous solution of antimony and potassium tartrate with syrup and gradually adding fluidextract of senega and fluidextract of squill, previously mixed, and finally adding sufficient syrup to make up the required volume. Each Cc. contains 0.002 Gm. of antimony and potassium tartrate.
Syrupus Senegæ	Syrup of Senega	Made by mixing fluidextract of senega with syrup.
Syrupus Sennæ	Syrup of Senna	Made by mixing fluidextract of senna with oil of coriander and adding sufficient syrup to make up the required volume.

Latin name.	English name.	Method of preparation.
Syrupus Tolutanus .	Syrup of Tolu .	Made by triturating tincture of tolu with magnesium carbonate, some sugar, and water, filtering the mixture, and dissolving sugar in the filtrate with the aid of gentle heat.
Syrupus Zingiberis .	Syrup of Ginger	Made by triturating a mixture of fluidextract of ginger and alcohol with magnesium carbonate, some sugar and water, filtering the mixture, and dissolving sugar in the filtrate with the aid of gentle heat.

Alphabetical List of National Formulary Syrups.

Latin name.	English name.	Method of Preparation.
Syrupus Allii . . .	Syrup of Garlic	Made by extracting sliced and bruised garlic by maceration with diluted acetic acid, and dissolving sugar in the filtrate.
Syrupus Althææ . .	Syrup of Althæa	Made by dissolving sugar in an infusion of althæa root, made with cold water and alcohol, dissolving sugar in the strained liquid, and adding glycerin, and finally sufficient water to make the required volume.
Syrupus Ammonii Hypophosphitis . .	Syrup of Ammonium Hypophosphite . . .	Made by adding an aqueous solution of ammonium hypophosphite to syrup, together with glycerin, diluted hypophosphorous acid and compound spirit of vanillin.
Syrupus Asari Compositus	Compound Syrup of Asarum (Compound syrup of Canada Snakeroot or Wild Ginger) . .	Made by adding to a hydroalcoholic tincture of asarum, potassium carbonate and cochineal, prepared by percolation, fluidextract of ipecac, and water, and dissolving sugar in the mixture by agitation.
Syrupus Bromidorum	Syrup of the Bromides . . .	Made by adding tincture of vanilla and syrup to a solution of the bromides of ammonium, calcium, lithium, potassium, and sodium in compound syrup of sarsaparilla. Compound tincture of cudbear is also added to improve the color.
Syrupus Calcii Hydrochlorophosphatis .	Syrup of Calcium Hydrochlorophosphate .	Made by adding to a solution of calcium phosphate in water and hydrochloric acid some tincture of fresh lemon peel, filtering the mixture, and adding to the filtrate sufficient syrup to make up the required volume.
Syrupus Calcii et Sodii Hypophosphitum	Syrup of Calcium and Sodium Hypophosphites .	Made by dissolving the hypophosphites of calcium and sodium in water, adding hypophosphorous acid, filtering, and dissolving sugar in the filtrate.
Syrupus Calcii Hypophosphitis . . .	Syrup of Calcium Hypophosphite	Made by dissolving calcium hypophosphite in water and hypophosphorous acid, filtering, and dissolving sugar in the filtrate.

Latin name.	English name.	Method of preparation.
Syrupus Calcii Iodidi	Syrup of Calcium Iodide	Made by preparing a solution of ferrous iodide and dissolving additional iodine therein. After heating some distilled water to boiling, alternate portions of calcium carbonate and the above iodized ferrous iodide solution are added and the heat continued until the mixture boils quietly, after which it is filtered and sugar dissolved in the filtrate by agitation.
Syrupus Calcii Lactophosphatis et Ferri	Syrup of Calcium Lactophosphate and Iron	Made by preparing a solution of ferrous lactate and potassium citrate in water and adding this to syrup of calcium lactophosphate.
Syrupus Cimicifugæ Compositus (Syrupus Actææ Compositus)	Compound Syrup of Cimicifuga (Compound Syrup of Actaæ, Compound Syrup of Black Cohosh)	Made by adding the fluidextracts of cimicifuga, ipecac, licorice, and senega to an infusion of wild cherry, then filtering the mixture with the aid of purified talc and dissolving sugar in the filtrate.
Syrupus Cinnamomi	Syrup of Cinnamon	Made by percolating Saigon cinnamon with a mixture of alcohol and cinnamon water and dissolving sugar in the percolate.
Syrupus Codeinæ	Syrup of Codeine	Made by dissolving codeine sulphate in syrup.
Syrupus Eriodictyi Aromaticus (Syrupus Corrigens)	Aromatic Syrup of Eriodictyon (Aromatic Syrup of Yerba Santa)	Made by dissolving the oils of clove, lemon and sassafras in alcohol, and adding fluidextract of eriodictyon, solution of potassium hydroxide, water and magnesium carbonate; after filtration, sugar is dissolved in the filtrate with the aid of moderate heat.
Syrupus Ferri et Mangani Iodidi	Syrup of Iodide of Iron and Manganese	Made by preparing separate solutions of ferrous iodide and manganese iodide, the latter by decomposition of manganese sulphate with sodium iodide in hydroalcoholic solution, and dissolving sugar in the mixed solutions by agitation.
Syrupus Ferri Hypophosphitis	Syrup of Ferric Hypophosphite	Made by dissolving ferric hypophosphite in distilled water with the aid of potassium citrate, adding orange flower water and dissolving sugar in the filtered liquid with the aid of heat.
Syrupus Ferri Lacto-Phosphatis	Syrup of Lactophosphate of Iron	Made by dissolving ferrous lactate in water with the aid of phosphoric acid and adding syrup to the solution.
Syrupus Ferri Protochloridi	Syrup of Protochloride of Iron (Syrup of Ferrous Chloride)	Made by mixing solution of ferrous chloride with glycerin, orange flower water, and syrup.
Syrupus Ferri, Quininæ et Strychninæ Phosphatum	Syrup of the Phosphates of Iron, Quinine and Strychnine	Made by dissolving ferric phosphate, quinine and strychnine in water and phosphoric acid; after filtering the solution into glycerin, syrup is added.

Latin name.	English name.	Method of preparation.
Syrupus Ferri Saccharati Solubilis (Syrupus Ferri Oxydati Solubilis)	Syrup of Soluble Saccharated Iron (Syrup of Saccharated Oxide of Iron. Syrup of Soluble Oxide of Iron) . . .	Made by dissolving saccharated oxide of iron in a mixture of syrup and water.
Syrupus Ficorum Compositus	Compound Syrup of Figs. . .	Made by digesting figs with water, straining and evaporating the infusion, and, while still warm, dissolving sugar therein; when cold, fluidextract of senna, aromatic fluidglycerate of cascara sagrada, oil of fennel and spirit of peppermint are added, and finally sufficient water to make up the required volume.
Syrupus Glycyrrhizæ	Syrup of Glycyrrhiza (Syrup of Licorice) . .	Made by mixing fluidglycerate of licorice with syrup.
Syrupus Hypophosphitum Compositus	Compound Syrup of Hypophosphites . . .	Made by dissolving sugar in an aqueous solution of the hypophosphites of calcium, potassium, sodium, iron, manganese, quinine and strychnine, together with sodium citrate, diluted hypophosphorous acid and glycerin.
Syrupus Iodotannicus	Syrup of Iodo-Tannin . .	Made by heating a mixture of iodine in powder, distilled water and tannic acid on a waterbath, at a temperature not exceeding 50° C. (122° F.) until combination is complete; sugar is then dissolved in the warm liquid and sufficient distilled water added to make up the required volume.
Syrupus Ipecacuanhæ et Opii	Syrup of Ipecac and Opium (Syrup of Dover's Powder) . .	Made by mixing tincture of ipecac and opium with spirit of cinnamon, cinnamon water, and syrup. Each mil. (or Cc.) represents about 0.085 Gm. of Dover's Powder or 0.0085 Gm. each of ipecac and opium.
Syrupus Krameriæ .	Syrup of Krameria (Syrup of Rhatany) . . .	Made by mixing fluidextract of krameria with syrup.
Syrupus Mannæ . . .	Syrup of Manna	Made by dissolving manna in hot water, adding alcohol, and filtering after 12 hours; finally dissolving sugar in the filtrate with aid of gentle heat.
Syrupus Morphinæ et Acaciæ (Syrupus Pectoralis)	Syrup of Morphine and Acacia (Jackson's Pectoral Syrup)	Made by dissolving morphine hydrochloride in syrup of acacia and adding oil of sassafras to the solution.
Syrupus Papaveris .	Syrup of Poppy	Made by exhausting poppy capsules, free from seeds and in coarse powder, by percolation with hot water, concentrating and filtering the percolate, and dissolving sugar in the filtrate while still warm; finally sufficient water is added to make up the required volume.

Latin name.	English name.	Method of preparation.
Syrupus Phosphatum Compositum . .	Compound Syrup of Phosphates (Chemical Food) . . .	Made by mixing compound solution of phosphates with syrup and glycerin, and coloring the mixture with tincture of cudbear.
Syrupus Phosphatum cum Quinina et Strychnina (Syrupus Hydrochlorophosphatum Compositus)	Syrup of Phosphates with Quinine and Strychnine (Compound Syrup of Hydrochlorophosphates . .	Made by dissolving quinine hydrochloride and strychnine nitrate in glycerin with the aid of heat, adding compound solution of phosphates, and finally sufficient syrup to make up the required volume.
Syrupus Pini Strobi Compositus . .	Compound Syrup of White Pine	Made by percolating white pine bark, wild cherry, spikenard, sanguinaria, sassafras, and balm of Gilead buds with a menstruum of alcohol, glycerin and water; sugar is dissolved in the percolate and lastly chloroform and oil of sassafras are added and sufficient water to make up the required volume.
Syrupus Pini Strobi Compositus cum Morphina . . .	Compound Syrup of White Pine with Morphine	Made by dissolving morphine sulphate in compound syrup of white pine.
Syrupus Quinidinæ .	Syrup of Quinidine (Bitterless Syrup of Quinidine) . . .	Made by mixing crystals of quinidine alkaloid and oil of orange with syrup and shaking the mixture thoroughly.
Syrupus Rhamni Catharticæ (Syrupus Spinæ Cervinæ) .	Syrup of Rhamnus Cathartica (Syrup of Buckthorn Berries)	Made by adding the oils of fennel and cinnamon to fluidextract of rhamnus cathartica and then adding sufficient syrup to make up the required volume.
Syrupus Rosæ . .	Syrup of Rose .	Made by mixing fluidextract of rose with water and diluted sulphuric acid and after 2 hours filtering the mixture; sugar is dissolved in the filtrate and finally sufficient water is added to make up the required volume.
Syrupus Rubi . .	Syrup of Rubus (Syrup of Blackberry Root) .	Made by mixing fluidextract of rubus with syrup.
Syrupus Rubi Fructus	Syrup of Blackberry Fruit .	Made by expressing the juice from garbled ripe blackberries, straining the same and adding sugar; the mixture is heated until it just boils, strained and bottled while hot.
Syrupus Rubi Idæi	Syrup of Raspberry . . .	Made by expressing the juice from fresh ripe raspberries, allowing the same to ferment at 20° C. until the filtered juice mixes clear with half its volume of alcohol; after straining, the juice is heated to the boiling point, the scum removed, the juice filtered while hot and sugar dissolved in the liquid with agitation.
Syrupus Sanguinariæ	Syrup of Sanguinaria (Syrup of Bloodroot) .	Made by percolating sanguinaria with acetic acid and water and dissolving sugar in the percolate.

Latin name.	English name.	Method of preparation.
Syrupus Sennæ Aromaticus	Aromatic Syrup of Senna	Made by percolating jalap, rhubarb, cinnamon, cloves, nutmeg, and oil of lemon with diluted alcohol, adding fluidextract of senna to the percolate, and dissolving sugar in the mixture.
Syrupus Sennæ Compositus	Compound Syrup of Senna	Made by mixing the fluidextracts of senna, rhubarb, and frangula with methyl salicylate dissolved in alcohol, and then adding sufficient syrup to make up the required volume.
Syrupus Sodii Hypophosphitis	Syrup of Sodium Hypophosphite	Made by dissolving sodium hypophosphite in water and hypophosphorous acid and dissolving sugar in the liquid by agitation.
Syrupus Stillingiæ Compositus	Compound Syrup of Stillingia	Made by mixing compound fluidextract of stillingia with glycerin and syrup.

Syrups used in pharmacy may be conveniently divided into two classses, namely, those possessing little or no medicinal properties and chiefly used for flavoring purposes, and those used as therapeutic agents and conveniently termed medicated syrups.

To the first class, or flavoring syrups, belong the following:

Syrup, Syrup of Blackberry Fruit, Syrup of Cinnamon, Syrup of Citric Acid, Syrup of Eriodictyon (Aromatic), Syrup of Ginger, Syrup of Orange, Syrup of Orange Flowers, Syrup of Raspberry.

The class of medicated syrups embraces the remaining syrups, namely:

Syrup of Acacia, Syrup of Althæa, Syrup of Ammonium Hypophosphite, Syrup of Asarum (Compound), Syrup of Bromides, Syrup of Calcium and Sodium Hypophosphites, Syrup of Calcium Hydrochlorophosphate, Syrup of Calcium Hypophosphite, Syrup of Calcium Iodide, Syrup of Calcium Lactophosphate, Syrup of Calcium Lactophosphate and Iron, Syrup of Cimicifuga (Compound), Syrup of Codeine, Syrup of Ferric Hypophosphite, Syrup of Ferrous Lactophosphate, Syrup of Ferrous Chloride, Syrup of Ferrous Iodide, Syrup of Figs (Compound), Syrup of Garlic, Syrup of Hydriodic Acid, Syrup of Hypophosphites, Syrup of Hypophosphites (Compound), Syrup of Iodo-tannin, Syrup of Ipecac, Syrup of Ipecac and Opium, Syrup of Iron and Manganese Iodide, Syrup of Krameria, Syrup of Lactucarium, Syrup of Licorice, Syrup of Manna, Syrup of Morphine and Acacia, Syrup of Phosphates (Compound), Syrup of Phosphates with Quinine and Strychnine, Syrup of Phosphates of Iron, Quinine and Strychnine Syrup of Poppy, Syrup of Quinidine, Syrup of Rhamnus Cathartica, Syrup of Rhubarb, Syrup of Rhubarb (Aromatic), Syrup of Rose, Syrup of Rubus, Syrup of Sanguinaria, Syrup of Sarsaparilla (Compound), Syrup of Senega, Syrup of Senna, Syrup of Senna (Aromatic), Syrup of Senna (Compound), Syrup of Sodium Hypophosphite, Syrup of Soluble Saccharated Iron, Syrup of

Squill, Syrup of Squill (Compound), Syrup of Stillingia (Compound), Syrup of Tar, Syrup of Tolu, Syrup of White Pine (Compound), Syrup of White Pine (Compound) with Morphine, Syrup of Wild Cherry.

Of the 67 syrups recognized in the U. S. Pharmacopœia and the *National Formulary*, 51 are directed to be made without the use of heat, and of these 30 are simple mixtures of syrup and the respective flavoring or medicinal agents usually in the form of solution. Of the remaining syrups, 3 are prepared by heating the solvent and sugar together to the boiling point; in 10 syrups the sugar is dissolved with the aid of a gentle heat, and in the case of 3 syrups, solution of the sugar is effected by means of waterbath heat, the temperature not being specified but necessarily below the boiling point of the mixture.

Classification of Syrups According to the Mode of Preparation.

Made by Adding the Flavoring or Medicinal Substance Direct to Syrup.

Syrup of Citric Acid, Syrup of Hydriodic Acid, Syrup of Lactucarium, Syrup of Rhubarb, Syrup of Rhubarb (Aromatic), Syrup of Sarsaparilla (Compound), Syrup of Senega, Syrup of Senna, Syrup of Squill (Compound).—U. S.

Syrup of Ammonium Hypophosphite, Syrup of Bromides, Syrup of Calcium Hydrochlorophosphate, Syrup of Calcium Lactophosphate and Iron, Syrup of Codeine, Syrup of Ferrous Chloride, Syrup of Ipecac and Opium, Syrup of Iron Lactophosphate, Syrup of Iron, Quinine and Strychnine Phosphates, Syrup of Krameria, Syrup of Licorice, Syrup of Morphine and Acacia, Syrup of Phosphates (Compound), Syrup of Phosphates with Quinine and Strychnine, Syrup of Quinidine, Syrup of Rhamnus Cathartica, Syrup of Rubus, Syrup of Senna (Compound), Syrup of Soluble Saccharated Iron, Syrup of Stillingia (Compound), Syrup of White Pine (Compound) with Morphine.—Nat. Form.

Made by Dissolving the Sugar without Heat.

Syrup, Syrup of Hypophosphites, Syrup of Calcium Lactophosphate, Syrup of Ipecac, Syrup of Orange, Syrup of Orange Flowers, Syrup of Tar, Syrup of Wild Cherry.—U. S.

Syrup of Althæa, Syrup of Asarum (Compound), Syrup of Calcium and Sodium Hypophosphites, Syrup of Calcium Hypophosphite, Syrup of Calcium Iodide, Syrup of Cimicifuga (Compound), Syrup of Cinnamon, Syrup of Garlic, Syrup of Hypophosphites (Compound), Syrup of Iron and Manganese Iodide, Syrup of Rose, Syrup of Sodium Hypophosphite, Syrup of White Pine (Compound).—Nat. Form.

Made by Dissolving the Sugar with the Aid of Gentle Heat.

Syrup of Ginger, Syrup of Squill, Syrup of Tolu.—U. S.

Syrup of Eriodictyon (Aromatic), Syrup of Ferric Hypophosphite, Syrup of Figs (Compound), Syrup of Manna, Syrup of Poppy, Syrup of Sanguinaria, Syrup of Senna (Aromatic).—Nat. Form.

Made by Dissolving the Sugar with the Aid of Waterbath Heat.

Syrup of Acacia, Syrup of Ferrous Iodide.—U. S.

Syrup of Iodo-tannin.—Nat. Form.

Made by Heating the Mixture of Solvent and Sugar to Boiling Point.

Syrup of Blackberry Fruit, Syrup of Raspberry.—Nat. Form.

Syrups made by simple admixture of the respective fluidextract with syrup are prone to precipitate on standing, owing to a change in the alcoholic strength of the fluid. While the official directions are suitable for extemporaneous preparation of the syrups, it will be found preferable, if the syrups are to be kept in stock, to dilute the respective fluidextract with water, setting the mixture aside for twenty-four hours and then filtering; finally the sugar may be dissolved in the clear filtrate either by agitation or percolation. In the author's experience syrups thus prepared keep well.

SPECIAL REMARKS.

Syrupus.—Official simple syrup contains 64.74 per cent. by weight of sugar, each mil. (or Cc.) representing 0.85 Gm.; it should be made with distilled water, so as to produce a solution of crystalline clearness, and if heat be employed, the syrup should be passed through a small dry strainer, which is then washed with sufficient distilled water used for rinsing the vessel to bring the volume up to the required quantity. Simple syrup should be made and preserved with care. One pound measures very nearly 12 fluidounces.

Syrupus Acaciæ.—Syrup of acacia or syrup of gum arabic is prone to spoil, especially in warm weather, and should be preserved in previously sterilized small bottles in a cold place. Solution of the acacia will be materially facilitated if the distilled water be heated before the gum is added and the mixture then frequently stirred. If small quantities of the syrup are to be made extemporaneously, 3 Gms. (or 50 grains) of clean granulated acacia may be triturated with 6 mils. (or Cc.) (or 1½ fluidrachms) of distilled water until dissolved, and then mixed with sufficient syrup to produce 30 mils. (or Cc.) (or 1 fluidounce) of finished product.

Syrupus Acidi Citrici.—Syrup of citric acid, made by mixing tincture of fresh lemon peel and a solution of citric acid with simple syrup, is an excellent substitute for lemon syrup, being more stable and of uniform acidity. It is of pleasant flavor and slightly opalescent, each mil. (or, Cc.) containing 0.010 Gm. of citric acid. Unfortunately, syrup of citric acid, when kept on hand for some time, acquires a terebinthinate odor; it should therefore be made in small quantities.

Syrupus Acidi Hydriodici.—Syrup of hydriodic acid is intended by the present official formula to be made extemporaneously, with the view of avoiding discoloration. If the acid liquid is kept in contact with the syrup for some length of time, especially in warm weather, caramelization of the sugar will take place and the syrup becomes colored, growing gradually darker. Syrup of hydriodic acid having more than a pale-straw color should not be dispensed. It contains 1.375 Gms. of hydrogen iodide (HI) in each 100 mils. (or Cc.), which is equivalent to very nearly 6.3 grains in each fluidounce.

Syrupus Althææ (*Syrup of Althæa*, also known as *Syrup of Marshmallow Root*).—Like syrup of acacia, this syrup does not keep well, especially in warm weather. The addition of alcohol to the water used for preparing the mucilage is for the purpose of preventing fermentation during the time of maceration. The finished syrup contains 10 per cent. by volume of glycerin and between 2 and 3 per cent. of alcohol.

Syrupus Aurantii.—Syrup of orange is made from tincture of fresh orange peel by triturating the same with purified talc and water, and filtering the milky mixture; the filter is washed with more water until a definite volume of clear filtrate is obtained, in which the citric acid and sugar are dissolved by agitation. The finished syrup has a pleasant aroma and an acidulous taste, and mixes clear with aqueous liquids. Syrup of orange should never be made from fluidextract of sweet orange peel, as the latter is prepared from dried peel with a hydroalcoholic menstruum, is without the fine orange flavor, and is more or less bitter; moreover, syrup of orange thus made turns liquids containing iron preparations dark, on account of the tannin in the fluidextract, which is not the case with the official syrup.

Syrupus Aurantii Florum.—Syrup of orange flowers contains the same proportion of sugar as simple syrup; it is made without the aid of heat, most conveniently by percolation.

Syrupus Calcii Iodidi (*Syrup of Calcium Iodide*).—A solution of ferrous iodide is first prepared from iron wire and iodine, which is then decomposed by addition of calcium carbonate, while the mixture is kept hot. Calcium iodide and ferrous carbonate are formed, the former remaining in solution; after removal of the iron carbonate by filtration, sugar is dissolved in the clear filtrate.

Syrupus Calcii Lactophosphatis.—Syrup of calcium lactophosphate, sometimes erroneously called syrup lactophosphate of lime, is easily prepared according to the official directions. The calcium carbonate

should be added very gradually to the diluted lactic acid so that a perfect solution may result. When the phosphoric acid is to be added this should be diluted with more water than officially directed (at least twice as much water as acid should be used), and this mixture must be added slowly to the solution of calcium lactate previously prepared, constantly stirring with a glass rod, so as to avoid precipitation of calcium phosphate. The newly formed salt will be kept in solution by the excess of phosphoric acid and the lactic acid present, or will be dissolved almost immediately after it has been precipitated. The acid solution, after addition of more water, is filtered, and to the filtrate the orange flower water and sugar are added, and the whole shaken until perfect solution has been effected. When freshly prepared, syrup of calcium lactophosphate is a colorless solution, but, like all syrups containing acid, it gradually becomes discolored, if kept on hand for some time, especially in warm weather; it should, therefore, not be made in large quantities and should be kept in a cool place. Each mil. (or Cc.) of the finished syrup represents 0.02584 Gm. of tricalcium phosphate.

Syrupus Eriodictyi Aromaticus (*Aromatic Syrup of Eriodictyon*, also known as *Aromatic Syrup of Yerba Santa*).—Solution of potassium hydroxide is added to prevent precipitation of resin when the water is mixed with the fluidextract of eriodictyon. A clear filtrate should be obtained, in which the sugar is dissolved without the aid of heat.

Syrupus Ferri et Mangani Iodidi (*Syrup of Iron and Manganese Iodide*).—A solution of ferrous iodide having been prepared from iron wire and iodine, is filtered upon sugar and to this is added a solution of manganese iodide made by decomposition of a solution of manganese sulphate with sodium iodide; the resulting sodium sulphate from the last reaction is precipitated by the alcohol present and the filtrate thus contains only the manganese iodide. Finally the sugar is dissolved without the aid of heat in the clear liquid.

Syrupus Ferri Hypophosphitis (*Syrup of Ferric Hypophosphite*).—The addition of potassium citrate is necessary to insure perfect solution of the ferric salt, which is but slightly soluble in water.

Syrupus Ferri Iodidi.—The first step in making syrup of ferrous iodide is the preparation of a solution of iodide of iron, and care should be taken that no iodine is lost and that a pale-green solution free from all iodine odor be obtained. This is then protected by addition of sugar and filtered into the remainder of the sugar, the flask and filter being rinsed with an additional quantity of distilled water. The sugar is dissolved by heating on a waterbath and the syrup then strained, the diluted hypophosphorous acid added, and finally sufficient distilled water to bring the weight up to the required quantity. The hypophosphorous acid, being a valuable reducing agent, is added to prevent oxidation and consequent discoloration of the syrup, and has been found superior to other agents. The official syrup of ferrous iodide contains 5 per cent. of ferrous iodide, which, as the specific gravity

of the syrup is 1.383 at 25° C., is equivalent to 6.91 Gms. in each 100 mils. (or Cc.).

Syrupus Ficorum Compositus (*Compound Syrup of Figs*).—This syrup is evidently intended to replace a largely advertised proprietary preparation, and owes its laxative properties chiefly to the fluidextract of senna and fluidglycerate of cascara sagrada present.

Syrupus Hypophosphitum (*Syrup of Hypophosphites*).—By this name the Pharmacopœia recognizes a syrup of the hypophosphites of calcium, potassium, and sodium; it is prepared by making a solution of the three salts in water, acidulating the same with hypophosphorous acid, adding glycerin, and then dissolving sugar in the liquid by agitation. Each Cc. of the syrup contains 0.045 Gm. of calcium hypophosphite, 0.015 Gm. each of potassium and sodium hypophosphite, and 0.002 Gm. of diluted hypophosphorous acid.

Syrupus Iodotannicus (*Syrup of Iodo-tannin*).—Iodine and tannin are capable of forming a dark amber-colored solution in water with the aid of heat, and the sugar should not be added until the absence of free iodine has been shown by testing with starch solution.

Syrupus Ipecacuanhæ (*Syrup of Ipecac*).—The object of the official directions to mix the fluidextract of ipecac with water and acetic acid is to bring the active principles of ipecac into a permanent solution as acetates and to reject those undesirable constituents of the fluidextract which are apt to cause the formation of flocculi in the syrup. The addition of glycerin to the filtered liquid still further preserves the preparation, after solution of the sugar, either by agitation or percolation. Each mil. (or Cc.) of the finished syrup represents 0.070 mil. (or Cc.) of the fluidextract of ipecac.

Syrupus Lactucarii (*Syrup of Lactucarium*).—The character of the finished syrup will depend upon that of the tincture of lactucarium used; if the latter has been carefully made so as to be free from the caoutchouc-like constituent of the drug, the resulting syrup should be clear and of a light-brownish color, otherwise a turbid mixture will result. Each mil. (or Cc.) of the syrup represents the active virtues of 0.05 Gm. of lactucarium.

Syrupus Picis Liquidæ (*Syrup of Tar*).—The preliminary washing of the tar, intended to remove certain water-soluble impurities, heretofore directed, has been omitted in the official formula. In order to obtain a clear solution, the tar is now dissolved in alcohol, mixed with magnesium carbonate and sugar, and after trituration with water, is allowed to stand for two hours with frequent stirring and then filtered. The sugar may be dissolved in the clear filtrate either by agitation or percolation. Each mil. (or Cc.) of the finished syrup represents 0.005 Gm. of tar.

Syrupus Pruni Virginianæ (*Syrup of Wild Cherry*).—The official directions to moisten the wild cherry bark with a mixture of water and glycerin, then to pack firmly in a percolator, saturate with more of the same menstruum and macerate for twenty-four hours, are for the

purpose of allowing reaction to go on between certain constituents of the bark, which results in the formation of hydrocyanic acid; the latter dissolves in the menstruum and is then extracted by slow percolation, water being gradually poured on top of the drug. The sugar may be dissolved by agitation or percolation. In the author's experience a No. 30 powder is preferable to the coarser powder ordered by the Pharmacopœia and permits of firmer packing of the moistened drug. The presence of glycerin in the menstruum yields a somewhat darker syrup and aids in its preservation. The amount of hydrocyanic acid present in the syrup is a very uncertain quantity, nor does it remain constant, owing to exposure and its volatile and unstable character.

Syrupus Rhei (*Syrup of Rhubarb*).—The official formula directs a solution of potassium carbonate to be added to fluidextract of rhubarb prior to its admixture with simple syrup; a small quantity of spirit of cinnamon is also added as a flavoring agent. The addition of an alkali prevents the separation of resinous matter by retaining the same in solution, and thus a clear syrup is obtained. The use of water for solution of the potassium carbonate appears quite unnecessary, since the alkali can be dissolved in a part of the simple syrup, and syrup of rhubarb thus prepared keeps admirably well. Each mil. (or Cc.) represents 0.100 Gm. of rhubarb.

Syrupus Rhei Aromaticus (*Aromatic or Spiced Syrup of Rhubarb*).—The object of adding potassium carbonate, which is readily soluble in the aromatic tincture of rhubarb, is to prevent precipitation of resinous matter, and thus produce a clear syrup.

Syrupus Sarsaparillæ Compositus (*Compound Syrup of Sarsaparilla*).—The formula for this popular syrup has been materially changed and simplified. A mixture of the fluidextracts of sarsaparilla, licorice and senna, to which has been added a solution of methyl salicylate, oil of anise and oil of sassafras in alcohol, is slowly added to syrup and then thoroughly mixed. Each mil. (or Cc.) of the finished syrup represents 0.200 Gm. of sarsaparilla and 0.015 Gm. each of senna and licorice root.

Syrupus Scillæ (*Syrup of Squill*).—On account of the acetic acid present in the vinegar of squill this syrup should always be made in glass or porcelain vessels, and all contact with metal should be avoided. Each mil. (or Cc.) of the syrup represents 0.045 Gm. of squill.

Syrupus Scillæ Compositus (*Compound Syrup of Squill*, also known as *Hive Syrup*).—As in the case of compound syrup of sarsaparilla, the formula for this syrup has been greatly simplified. Compound syrup of squill is now made by adding a mixture of fluidextract of senega and fluidextract of squill gradually to syrup to which has previously been added a solution of antimony and potassium tartrate in warm distilled water. Each mil. (or Cc.) of the finished product represents 0.080 Gm. each of senega and squill, and contains 0.002 Gm. of antimony and potassium tartrate.

Syrupus Senegæ (*Syrup of Senega*).—The present official formula for syrup of senega is admirably adapted for making small quantities extemporaneously, but the syrup has been found to precipitate more or less upon standing for some time, and the following modification is suggested for larger quantities: 200 mils. (or Cc.) of fluidextract of senega should be mixed with 350 mils. (or Cc.) of water and the mixture filtered after twenty-four hours; 680 Gms. of sugar may then be dissolved in the filtrate by agitation or percolation and sufficient water added to bring the volume of syrup up to 1000 mils. (or Cc.). The finished syrup contains about 12 per cent. of alcohol.

Syrupus Sennæ (*Syrup of Senna*).—The official process for making syrup of senna is well suited for extemporaneous use; however, like other syrups made by direct addition of a fluidextract to syrup, syrup of senna will frequently precipitate upon standing for some time, and a better preparation may be obtained by mixing the oil of coriander, 5 mils. (or Cc.) with 250 mils. (or Cc.) of fluidextract of senna, then adding 360 mils. (or Cc.) of water, shaking well, and setting aside for twenty-four hours. After filtering the mixture, 635 Gms. of sugar may be dissolved in the filtrate by agitation or percolation and enough water added to bring the volume up to 1000 mils. (or Cc.). The finished syrup contains about 12 per cent. of alcohol.

Syrupus Tolutanus (*Syrup of Tolu*).—The official formula for this syrup yields a very satisfactory product. The small amount of alcohol allowed to remain aids in keeping more of the balsamic and odorous principles in solution. The finished syrup is a colorless liquid having a decided odor and taste of tolu, which becomes less pleasant when the syrup is kept for some length of time. Each mil. (or Cc.) represents 0.01 Gm. of balsam of tolu.

Syrupus Zingiberis (*Syrup of Ginger*).—The addition of alcohol to the fluidextract of ginger is for the purpose of keeping more of the oleoresinous matter in solution in the aqueous liquid than would otherwise be the case. If carefully made, the official syrup has the characteristic aroma of ginger and a pleasant, slightly pungent taste. Each mil. (or Cc.) represents 0.03 Gm. of ginger.

CHAPTER XVII.

MUCILAGES, HONEYS, AND GLYCERITES.

MUCILAGES.

THE preparations recognized in pharmacy under this name are viscid, adhesive liquids formed by solution of mucilaginous principles in water; with one exception they are unstable and readily undergo putrefactive changes in warm weather, hence they should be freshly prepared when wanted. The 2 official mucilages are those of acacia and tragacanth.

Mucilago Acaciæ (*Mucilage of Acacia*).—The official directions require that acacia in small fragments be first washed with cold water and allowed to drain, for the purpose of removing foreign matter often adhering to the outer surface. For every 350 Gms. of acacia used, add enough warm distilled water to make the mixture weigh 1000 Gms. Securely stopper the container and agitate it from time to time until the acacia is dissolved. The official formula will produce quite a viscid liquid, containing 34 per cent. of acacia, each mil. (or Cc.) representing about 0.378 Gm., but the solution is weaker than the mucilage of the British and German pharmacopœias. Owing to the fact that the liquid becomes denser as solution progresses, agitation of the mixture will be found somewhat difficult, especially if large quantities are used, and it will be found more expedient to suspend the washed acacia in the distilled water, in a bag of loosely textured cloth, in a tightly closed wide-mouth jar, to be occasionally moved about in the liquid, so that fresh portions of the solvent may continually displace the solution formed and thus complete solution be more rapidly effected. Pieces of clear, white acacia should be selected for the mucilage, which, when made, should be preserved in completely filled bottles in a cool place.

Mucilago Tragacanthæ.—The official directions for preparing mucilage of tragacanth are, to add 6 Gms. of tragacanth to a boiling mixture of 18 Gms. of glycerin and 75 mils. (or Cc.) of water, and then macerate for twenty-four hours, with frequent stirring; after the addition of sufficient water to bring the weight of the mixture up to 100 Gms. it is beaten to a uniform consistence and then expressed through muslin. Mucilage of tragacanth forms a somewhat opaque semiliquid jelly, and the presence of the glycerin prevents decomposition. Tragacanth is only partially soluble in water, but absorbs the latter and swells to a gelatinoid mass.

The *National Formulary* also recognizes two mucilages, both of which must be prepared extemporaneously, as they do not keep well. They are as follows:

Mucilago Chondri	Mucilage of Irish Moss	Made by heating washed Irish moss with water on a boiling water-bath for fifteen minutes and then straining.
Mucilago Sassafras Medullæ	Mucilage of Sassafras Pith	Made by macerating sassafras pith in cold water for 3 hours and straining without expression. It must be freshly prepared when wanted.

HONEYS.

Clarified honey, or Mel Depuratum of the Pharmacopœia, is prepared by mixing honey with 2 per cent. of its weight of paper pulp and heating the mixture on a waterbath as long as scum rises to the surface; the scum is carefully removed with a skimmer and sufficient distilled water added to restore loss by evaporation, after which the mixture is strained and 5 per cent. of its weight of glycerin is added to the strained liquid for the purpose of better preservation.

Medicated honeys are simply mixtures of clarified honey with certain medicinal agents, and are, as a rule, prepared extemporaneously.

The following are used to some extent either by physicians or by the public without medical advice:

Mel Rosæ U. S. P.	Honey of Rose	Made by mixing fluidextract of rose with clarified honey, and contains in every 100 Gms. the astringent principles of 12 Gms. of red rose petals.
Mel Rosæ et Sodii Boratis Nat. Form.	Honey of Rose and Sodium Borate (Honey of Rose with Borax)	Made by mixing sodium borate with glycerin and adding honey of rose.
Mel Sodii Boratis Nat. Form.	Honey of Sodium Borate	Made by mixing sodium borate with glycerin and adding clarified honey.

GLYCERITES.

This valuable class of preparations consists of solutions of the medicinal agents in glycerin; they are permanent, and are readily miscible with water or alcohol.

THE GLYCERITES OF THE U. S. PHARMACOPŒIA.

Glyceritum Acidi Tannici (*Glycerite of Tannic Acid*).—Although tannic acid is perfectly soluble in cold glycerin, the solution of so large a proportion as directed in the official glycerite is best effected by the aid of heat. The Pharmacopœia directs that 80 Gms. of glycerin be

heated in a wide-mouthed bottle in a boiling waterbath and that 20 Gms. of tannic acid be then added in small portions, and the mixture agitated until the tannic acid is dissolved. In the author's experience, equally good results are obtained if the glycerin be heated in a porcelain dish on a boiling waterbath, the tannic acid in fine powder then added and the mixture stirred with a glass rod until perfect solution is effected. All contact with metal must be carefully avoided. When solution is completed, a deep green transparent liquid results, which should be strained while still warm through flannel or a pledget of cotton. Glycerite of tannic acid contains about 0.300 Gm. of tannic acid in each mil. (or Cc.), which is equal to about 120 grains in 1 fluidounce.

Glyceritum Amyli (*Glycerite of Starch*, also known as *Plasma*).—The official directions for preparing this glycerite are to triturate 10 parts of starch with 10 parts of water to a homogeneous mixture, adding this to 80 parts of glycerin heated to 140° C. and continuing the heat until a translucent jelly is formed. As starch usually occurs in lumps, it is necessary first to rub it in a mortar into a fine powder, which should be transferred to a porcelain capsule, and then mixed with the water to a smooth paste, after which the glycerin is added, so as to avoid loss, which is unavoidable if the mixture be made in the mortar; heat must be applied cautiously and the mixture *constantly* stirred with a thick glass rod or a wooden spatula, to avoid scorching and consequent discoloration. The liquid gradually thickens as the heat is increased, and the entire disappearance of white spots indicates perfect solution. The high heat, 140° C. (284° F.), indicated in the official formula is necessary to effect rupture of the starch granules, without which solution of the starch cannot take place; to insure uniform heating, wire gauze should invariably be interposed between the capsule and the flame. Glycerite of starch is hygroscopic, therefore it must be preserved in tightly closed jars, so as to avoid contact with air.

Glyceritum Boroglycerini (*Glycerite of Boroglycerin*).—The preparation of glycerite of boroglycerin, also known as glycerite of glyceryl borate, involves first the production of boroglycerin, or glyceryl borate, and secondly the solution of this compound in glycerin. When boric acid and glycerin are heated together to about 150° C. (302° F.) chemical action sets in, water being given off, while a new compound, glyceryl borate, is formed, which upon cooling is obtained as a transparent, almost colorless and very hygroscopic mass; the mixture must be frequently stirred to break up the constantly forming film, and care must be observed that the heat prescribed be neither exceeded nor continued longer than necessary, so as to avoid a yellowish or brownish coloration. Thirty-one parts of boric acid and 46 parts of glycerin will unite to form 50 parts of glyceryl borate; hence in the official process the reaction is known to be complete when the weight of the mixture has been reduced to 500 Gms.; then, while still hot, an equal weight of glycerin is added and thoroughly incorporated, thus

making a 50 per cent. solution of boroglycerin. Each mil. (or Cc.) contains about 0.683 Gm. of boroglycerin, which is equal to about 312 grains in 1 fluidounce.

Glyceritum Hydrastis (*Glycerite of Hydrastis*, also known as *Glycerite of Golden Seal*).—In the official process for this glycerite, 1000 Gms. of finely powdered hydrastis root are exhausted with alcohol by percolation. The alcohol is then nearly all recovered from the percolate by distillation, and the thick, concentrated liquid is poured into 500 mils. (or Cc.), of ice-cold water and set aside for twenty-four hours in a cold place. After filtration, a portion of the filtrate is assayed and from the results thus obtained the amount of ether-soluble alkaloids in the remainder of the liquid is calculated. Enough cold water is then added, so that when mixed with an equal volume of glycerin, the mixture shall contain 1.25 Gms. of the ether-soluble alkaloids in every 100 mils. (or Cc.). Finally the necessary quantity of glycerin is added and the whole thoroughly mixed. The permissible limit of variation from the official standard has been fixed at 10 per cent. namely, not less than 1.12 Gms. nor more than 1.37 Gms. of ether-soluble alkaloids in 100 mils. (or Cc.).

Glycerite of hydrastis is of about two-thirds the alkaloidal strength of the official fluidextract of hydrastis, but possesses the advantage of being miscible with water in all proportions without precipitation.

The object of removing the alcohol by distillation and then pouring the residue into ice water, is to get rid of the soft resinous matter extracted from the root, which possesses no medicinal virtues and is immiscible with water.

Glyceritum Phenolis (*Glycerite of Phenol*, also known as *Glycerite of Carbolic Acid*.)—The Pharmacopœia directs this glycerite to be made by mixing 1 volume of liquefied phenol with 4 volumes of glycerin. The official liquefied phenol, being made by adding 10 grams of water to 90 grams of melted phenol, should contain not less than 87 per cent. of absolute phenol, and hence each mil. (or Cc.) of the glycerite will contain about 0.185 Gm. of pure phenol or carbolic acid. It is readily soluble in water.

THE GLYCERITES OF THE NATIONAL FORMULARY.

The *National Formulary* recognizes the following glycerites:

Glyceritum Bismuthi (*Glycerite of Bismuth*).—This glycerite is prepared by first making a solution of bismuth trinitrate from bismuth subnitrate, nitric acid, and water; to this tartaric acid is added and then sodium bicarbonate, which causes precipitation of bismuth tartrate. The precipitate, having been well washed, is dissolved in a strong solution of sodium tartrate, and after filtration glycerin is added as a preservative. The glycerite contains about 16 grains of bismuth and sodium tartrate in each fluidrachm; it keeps for any length of time and is used in the preparation of elixir of bismuth

and solution of bismuth. The finished product contains 50 per cent. by volume of glycerin.

Glyceritum Guaiaci (*Glycerite of Guaiac*).—Powdered guaiac is treated with a weak solution of potassium hydroxide, when combination of the resin and alkali takes place and solution results; to this solution, after filtration, glycerin is added. The finished product contains 60 per cent. by volume of glycerin.

Glyceritum Pepsini (*Glycerite of Pepsin*).—This glycerite is made by dissolving pepsin in a mixture of water and hydrochloric acid; after filtration, with the aid of purified talc, an equal volume of glycerin is added to the clear solution. It contains 50 per cent. by volume of glycerin.

Glyceritum Picis Liquidæ (*Glycerite of Tar*).—As tar contains water-soluble impurities, these are first removed by washing with cold water as long as the washings redden blue litmus paper. The washed tar is then triturated with alcohol, magnesium carbonate, glycerin, and water, added in the order named, and the mixture filtered, water being passed through the filter to make up the required volume. The glycerite contains 12½ per cent. of alcohol and 25 per cent. of glycerin, both by volume.

Glyceritum Tragacanthæ (*Glycerite of Tragacanth*).—This preparation is made by simple trituration of powdered tragacanth with glycerin and the subsequent addition of water, when, upon standing, a thick gelatinous paste is formed. It serves as an excellent excipient for certain pill masses.

Glyceritum Vitelli Ovi (*Glycerite of Yolk of Egg, Glyconin*).—A solution of fresh yolk of egg in glycerin. In order to obtain a satisfactory preparation the yolk of egg should be carefully separated from the albumen, and the membrane enclosing the yolk then ruptured, so that the pure yolk may run and be weighed; the glycerin should be added gradually with constant trituration. The finished product contains 55 per cent. by weight of glycerin, and should be preserved in tightly stoppered bottles, so as to prevent the absorption of moisture from the air.

The chief use of this glycerite is as an emulsifying agent for fixed and volatile oils, 1 fluidounce of the former, or ½ fluidounce of the latter, requiring 2½ fluidrachms of the glycerite.

CHAPTER XVIII.

ELIXIRS.

THE word "elixir" is said to be of ancient origin, and derived, according to Dr. Charles Rice, from two Arabic words, pronounced *al-iksir;* the Arabic *iksir* comes from the Greek ξήριον, meaning a dry powder, such as was used for dusting wounds. For a long time the word was applied by alchemists to the wonderful transformation powder used in the supposed conversion of base metals into silver and gold. Later on, the term was also applied to liquids, and used to designate certain compound tinctures for which rare medicinal properties were claimed. In this latter sense the term elixir is still used to some extent in Continental Europe, and, as a rule, such preparations are characterized by an unpleasant taste. In modern American pharmacy the word has come to mean an entirely different class of preparations, the distinguishing features of which are a pleasantly aromatic sweet taste, and the presence of alcohol varying in proportion from 20 to 25 per cent. by volume. Prior to 1865, only two elixirs of this kind were used to any extent in this country, namely, *Elixir of calisaya* and *Elixir of ammonium valerianate;* but through the efforts of enterprising manufacturers the list was rapidly augmented and reached its height between 1870 and 1875. A reaction, however, gradually set in, and at the present day many once popular elixirs have fallen into disuse. There can be no doubt that a sweet, aromatic, and slightly alcoholic liquid forms a pleasant vehicle for many remedies, but the presence of 25 per cent. of alcohol may in some instances be positively injurious, and, moreover, the active ingredients are frequently present in such small quantities as to render the medicinal value of the preparation doubtful.

While the Pharmacopœia recognizes but two elixirs, aromatic elixir and elixir of licorice, which are intended as vehicles for other drugs, the *National Formulary* gives directions for the preparation of 76 elixirs, of which many, more than half, can be prepared extemporaneously by simple solution of the medicinal ingredient in the desired vehicle, as, for instance, the elixirs of the alkali bromides, citrates, hypophosphites, and salicylates, elixir of iron pyrophosphate, ferrated elixir of gentian, etc.

It is often desirable to impart color to an elixir, but since not all coloring agents are equally well suited for acid and alkaline liquids, it becomes necessary to exercise proper discretion. For acid or neutral liquids the *National Formulary* recommends either the simple or compound tincture of cudbear, the former for a bright red and the

latter for a brownish-red tint; of either tincture, 2 fluidrachms will suffice to color a pint of elixir. For alkaline liquids, such as elixir of ammonium valerate, the coloring agent should be a solution of carmine, which is best prepared with the aid of ammonia water; the *National Formulary* furnishes a satisfactory formula for the same.

Elixirs should never be exposed to extremes of temperature and should always be dispensed perfectly clear.

THE ELIXIRS OF THE U. S. PHARMACOPŒIA.

Elixir Aromaticum (*Aromatic Elixir*, also known as *Elixir of Orange* and *Simple Elixir*).—The official directions for making this elixir are to mix compound spirit of orange, 12 mils. (or Cc.), with sufficient alcohol to produce 250 mils. (or Cc.); to this solution are added syrup, 375 mils. (or Cc.), in divided portions, shaking after each addition, and afterward, in the same manner, 375 mils. (or Cc.) of distilled water. On account of the turbidity caused by the solution of the volatile oils, when mixed with the aqueous liquids, 30 Gms. of purified talc are added to the mixture, the whole well shaken and then filtered through paper, passing enough of a mixture of alcohol, 1 volume, and water, 3 volumes, through the filter to bring the volume up to 1000 mils. (or Cc.).

Elixir Glycyrrhizæ, Elixir Adjuvans U. S. P. VIII Rev. (*Elixir of Glycyrrhiza, Elixir of Licorice*).—This preparation, made by mixing 1 volume of fluidextract of licorice with 7 volumes of aromatic elixir, has a sweet aromatic taste and is well adapted for disguising an unpleasant saline or bitter taste of drugs. It should never be used in connection with acid liquids, as these will cause precipitation.

Although the popular Elixir of the Phosphates of Iron, Quinine and Strychnine has been dropped from the Pharmacopœia and not introduced into the recently revised edition of the *National Formulary*, its use by physicians will no doubt continue, and for the benefit of those pharmacists who may still prefer to make this preparation, the following formula is inserted, which corresponds in strength to that of the last Pharmacopœia, but differs somewhat in the directions for manipulation, and has been successfully used by pharmacists in different parts of the country for many years: Carefully weigh 16 Gms. of acetic acid (36 per cent., U. S. P.), into a beaker, add 5.1 Gms. of ammonium carbonate, in firm translucent pieces, and when solution is complete add 350 mils. (or Cc.) of aromatic elixir and 2 mils. (or Cc.) of phosphoric acid. Dissolve 8.75 Gms. of quinine (alkaloid) and 0.275 Gm. of strychnine (alkaloid) in 40 mils. (or Cc.) of alcohol, add this solution to the acid mixture and rinse the beaker or flask with 20 mils. (or Cc.) of alcohol, adding this also to the previous mixture; now add sufficient aromatic elixir to bring the volume of the mixture up to 880 mils. (or Cc.). Dissolve 17.5 Gms. of phosphate of iron (soluble scale salt) in 30 mils. (or Cc.) of distilled water, with the

aid of heat, and when cool add sufficient aromatic elixir to bring the volume of solution up to 120 mils. (or Cc.). Finally mix the two solutions and keep the finished product in dark amber-colored bottles. Note: If the solution of iron phosphate shows an acid reaction with litmus paper, it should be neutralized nearly, but not entirely, by the cautious addition of ammonia water; experience has shown that under such conditions the elixir is less liable to darken materially.

If these directions be carefully followed, no precipitation whatever will occur and no difficulty will be experienced in obtaining a perfectly clear preparation, which is miscible with water in all proportions and keeps well at all seasons. The addition of ammonium acetate solution is necessary to prevent precipitation when the iron solution is added to the acid solution of the alkaloids. Care must be taken that an excess of ammonia water be not added to the iron solution, otherwise the color of the elixir becomes much darker, and, therefore, it is preferable to leave the iron solution slightly acid. Like all solutions of ferric phosphate, this elixir is prone to darken when exposed to light, and it should, therefore, be kept in a dark place and dispensed in dark-amber bottles. The above modifications were first suggested by E. A. Cornell, and have been found very satisfactory.

THE ELIXIRS OF THE NATIONAL FORMULARY.

The following list gives the titles and composition of the Elixirs of the *National Formulary:*

Elixir Ammonii Bromidi (*Elixir of Ammonium Bromide*).—A solution of ammonium bromide in a mixture of syrup, distilled water, and aromatic elixir.

Elixir Ammonii Valeratis (*Elixir of Ammonium Valerate*).—A faintly alkaline solution of ammonium valerate in aromatic elixir, flavored with tincture of vanilla and colored with compound tincture of cudbear. It alsc contains a very small quantity, 0.15 per cent. by volume, of chloroform.

Elixir Amygdalæ Compositum (*Compound Elixir of Almond*).—A solution of oil of bitter almond and vanillin in a mixture of orange flower water, alcohol, syrup, and water.

Elixir Anisi (*Elixir of Anise*).—A solution of anethol, oil of fennel, and spirit of bitter almond in alcohol, mixed with syrup and water and filtered after twelve hours with the aid of purified talc.

Elixir Aromaticum Rubrum (*Red Aromatic Elixir*).—The official aromatic elixir colored with cudbear.

Elixir Aurantii Amari (*Elixir of Bitter Orange*).—A mixture of oil of bitter orange, tincture of bitter orange peel, alcohol, orange flower water, syrup, and water, filtered clear with the aid of purified talc.

Elixir Bismuthi (*Elixir of Bismuth*).—A mixture of glycerite of bismuth, glycerin, water, and aromatic elixir.

Elixir Buchu (*Elixir of Buchu*).—A mixture of fluidextract of buchu, alcohol, and aromatic elixir, which is allowed to stand for twelve hours and then filtered with the aid of purified talc.

Elixir Buchu Compositum (*Compound Elixir of Buchu*).—A mixture of compound fluidextract of buchu, and aromatic elixir, which is allowed to stand for twelve hours and then filtered with the aid of purified talc.

Elixir Buchu et Potassii Acetatis (*Elixir of Buchu and Potassium Acetate*).—A solution of potassium acetate in elixir of buchu.

Elixir Calcii Bromidi (*Elixir of Calcium Bromide*).—A solution of calcium bromide and diluted hydrobromic acid in water, syrup, and aromatic elixir.

Elixir Calcii et Sodii Glycerophosphatum (*Elixir of Calcium and Sodium Glycerophosphates*).—A solution of the glycerophosphates of calcium and sodium, and phosphoric acid, in a mixture of distilled water, glycerin, and aromatic elixir.

Elixir Calcii Hypophosphitis (*Elixir of Calcium Hypophosphite*).—A solution of calcium hypophosphite and hypophosphorous acid in aromatic elixir.

Elixir Calcii Lactophosphatis (*Elixir of Calcium Lactophosphate*).—A solution of calcium lactate and phosphoric acid in water, syrup and alcohol and flavored with compound spirit of orange.

Elixir Cardamomi Compositum (*Compound Elixir of Cardamom*).—A mixture of compound spirit of cardamom, alcohol, syrup, and water, filtered clear with the aid of purified talc.

Elixir Cascaræ Sagradæ (*Elixir of Cascara Sagrada.*)—A mixture of equal volumes of aromatic fluidextract of cascara sagrada and aromatic elixir.

Elixir Cascaræ Sagradæ Compositum (*Compound Elixir of Cascara Sagrada, Laxative Elixir*).—A mixture of aromatic fluidextract of cascara sagrada, fluidextract of senna, fluidextract of juglans, and aromatic elixir.

Elixir Catharticum Compositum (*Compound Cathartic Elixir*).—A mixture of the fluidextracts of frangula, rhubarb and senna with aromatic elixir, flavored with spirit of peppermint. A small quantity of solution of potassium hydroxide is added to the aromatic elixir before admixture of the fluidextracts to prevent precipitation.

Elixir Cinchonæ Alkaloidorum (*Elixir of Cinchona Alkaloids, Elixir of Calisaya (Alkaloidal)*).—A solution of the sulphates of quinine, cinchonidine, and cinchonine in aromatic elixir, colored with compound tincture of cudbear. Each mil. (or Cc.) contains 0.002 Gm. of quinine sulphate and 0.001 Gm. each of the sulphates of cinchonidine and cinchonine. This preparation was formerly also known as *Compound Elixir of Quinine.*

Elixir Cinchonæ Alkaloidorum et Ferri (*Elixir of Cinchona Alkaloids and Iron, Ferrated Elixir of Calisaya (Alkaloidal)*).—A mixture of an aqueous solution of ferric phosphate with elixir of cinchona alkaloids.

Elixir Cinchonæ Alkaloidorum et Hypophosphitum (*Elixir of Cinchona Alkaloids and Hypophosphites, Elixir of Calisaya (Alkaloidal) with Hypophosphites*).—A mixture of an aqueous solution of the hypophosphites of calcium and sodium, and hypophosphorous acid, with elixir of cinchona alkaloids.

Elixir Cinchonæ Alkaloidorum, Ferri, Bismuthi et Strychninæ (*Elixir of Cinchona Alkaloids, Iron, Bismuth and Strychnine, Elixir of Calisaya (Alkaloidal), with Iron, Bismuth, and Strychnine*).—A mixture of an aqueous solution of strychnine sulphate and elixir of cinchona alkaloids, iron and bismuth.

Elixir Cinchonæ Alkaloidorum, Ferri et Bismuthi (*Elixir of Cinchona Alkaloids, Iron and Bismuth, Elixir of Calisaya (Alkaloidal) with Iron and Bismuth*).—A mixture of glycerite of bismuth and elixir of cinchona alkaloids and iron.

Elixir Cinchonæ Alkaloidorum, Ferri et Calcii Lactophosphatis (*Elixir of Cinchona Alkaloids, Iron and Calcium Lactophosphate, Elixir of Calisaya (Alkaloidal), Iron and Lactophosphate of Lime*).—A mixture of syrup of calcium lactophosphate with a solution of potassium citrate in elixir of cinchona alkaloids and iron.

Elixir Cinchonæ Alkaloidorum, Ferri et Pepsini (*Elixir or Cinchona Alkaloids, Iron and Pepsin, Elixir of Calisaya (Alkaloidal) with Iron and Pepsin*).—A mixture of glycerite of pepsin and elixir of cinchona alkaloids and iron.

Elixir Cinchonæ Alkaloidorum, Ferri et Strychninæ (*Elixir of Cinchona Alkaloids, Iron and Strychnine, Elixir of Calisaya (Alkaloidal) with Iron and Strychnine*).—A mixture of an aqueous solution of strychnine sulphate and elixir of cinchona alkaloids and iron.

Elixir Corydalis Compositum (*Compound Elixir of Corydalis*).—A mixture of the fluidextracts of corydalis, stillingia, xanthoxylum, and iris with alcohol, in which potassium iodide has been dissolved, and aromatic elixir then added.

Elixir Eriodictyi Aromaticum, Elixir Corrigens (*Aromatic Elixir of Eriodictyon, Aromatic Elixir of Yerba Santa*).—A mixture of fluidextract of eriodictyon, pumice, magnesium carbonate, compound elixir of taraxacum and syrup is shaken frequently during two hours, allowed to stand over night and filtered. This elixir possesses little or no medicinal properties, and is used chiefly as a vehicle for quinine and other bitter remedies.

Elixir Ferri Hypophosphitis (*Elixir of Hypophosphite of Iron*).—A solution of hypophosphite of iron and potassium citrate in water, mixed with aromatic elixir.

Elixir Ferri Lactatis (*Elixir of Lactate of Iron*).—A solution of lactate of iron and potassium citrate in water mixed with aromatic elixir.

Elixir Ferri Phosphatis (*Elixir of Phosphate of Iron*).—A mixture of a strong solution of ferric phosphate in water with aromatic elixir.

Elixir Ferri Pyrophosphatis (*Elixir of Pyrophosphate of Iron*).—A mixture of a strong solution of ferric pyrophosphate in water with aromatic elixir.

Elixir Ferri Pyrophosphatis, Quininæ, et Strychninæ (*Elixir of Pyrophosphate of Iron, Quinine, and Strychnine*).—A solution of quinine sulphate and strychnine citrate in alcohol, flavored with oil of orange, and mixed with warm syrup to which is then added a solution of ferric pyrophosphate in water.

Elixir Ferri, Quininæ, et Strychninæ (*Elixir of Iron, Quinine, and Strychnine*).—A solution of quinine hydrochloride, strychnine sulphate and tincture of citro-chloride of iron in a mixture of alcohol, glycerin and water, flavored with compound spirit of orange, and filtered clear with the aid of purified talc.

Elixir Formatum (*Elixir of Formates*).—A mixture of a freshly prepared solution of the formates of potassium and sodium with aromatic elixir.

Elixir Formatum Compositum (*Compound Elixir of Formates*).—A mixture of a freshly prepared solution of the formates of lithium, magnesium, quinine, sodium and strontium with alcohol, glycerin and water, flavored with acetic ether and compound spirit of cardamom.

Elixir Gentianæ (*Elixir of Gentian*).—A mixture of fluidextract of gentian, alcohol, aqueous solution of sodium citrate, compound spirit of cardamom, syrup, glycerin and water, filtered clear with the aid of purified talc.

Elixir Gentianæ et Ferri (*Elixir of Gentian and Iron, Elixir of Gentian with Tincture of Ferric Citro-chloride*).—A mixture of elixir of gentian with tincture of citro-chloride of iron.

Elixir Gentianæ et Ferri Phosphatis, Elixir Gentianæ Ferratum (*Elixir of Gentian and Ferric Phosphate, Ferrated Elixir of Gentian*).—A mixture of a strong solution of ferric phosphate in water, with elixir of gentian.

Elixir Gentianæ Glycerinatum (*Glycerinated Elixir of Gentian*).—A mixture of the fluidextracts of gentian and taraxacum, phosphoric acid, tincture of sweet orange peel, compound tincture of cardamom, glycerin and acetic ether, with a solution of sugar in sherry wine. It is allowed to stand for twenty-four hours and then filtered.

Elixir Glycerophosphatum Compositum (*Compound Elixir of Glycerophosphates, Compound Solution of Glycerophosphates*).—A mixture of a solution of the glycerophosphates of calcium, iron, manganese, quinine, sodium and strychnine, and lactic acid, with alcohol, glycerin and water, flavored with compound spirit of cardamom and filtered clear with the aid of purified talc.

Elixir Glycyrrhizæ Aquosum (*Aqueous Elixir of Glycyrrhiza, Aqueous Elixir of Licorice*).—A mixture of fluidextract of licorice, compound spirit of cardamom, orange flower water, glycerin, syrup, and water.

Elixir Glycyrrhizæ Aromaticum (*Aromatic Elixir of Glycyrrhiza, Aromatic Elixir of Licorice*).—A mixture of fluidextract of licorice and aromatic elixir, flavored with the oils of cassia, clove, fennel, and nutmeg.

Elixir Guaranæ (*Elixir of Guarana*).—A mixture of fluidextract of guarana, aromatic elixir, and compound elixir of taraxacum. It is allowed to stand for twenty-four hours and then filtered.

Elixir Humuli (*Elixir of Humulus, Elixir of Hops*).—A mixture of fluidextract of hops, compound elixir of taraxacum, and aromatic elixir, flavored with tincture of vanilla. After addition of some purified talc, it is allowed to stand for twenty-four hours and then filtered.

Elixir Hypophosphitum (*Elixir of Hypophosphites*).—A solution of the hypophosphites of calcium, potassium, and sodium, and hypophosphorous acid, in water, mixed with glycerin, compound spirit of cardamom, and aromatic elixir.

Elixir Hypophosphitum cum Ferro (*Elixir of Hypophosphites with Iron*).—An aqueous solution of the hypophosphites of calcium, iron, potassium and sodium, and hypophosphorous acid, to which are added syrup and aromatic elixir.

Elixir Lithii Bromidi (*Elixir of Lithium Bromide*).—A mixture of an aqueous solution of lithium bromide, syrup, and aromatic elixir.

Elixir Lithii Citratis (*Elixir of Lithium Citrate*).—A solution of lithium citrate in aromatic elixir.

Elixir Lithii Salicylatis (*Elixir of Lithium Salicylate*).—A solution of lithium salicylate in aromatic elixir.

Elixir Pepsini (*Elixir of Pepsin*).—A mixture of glycerite of pepsin, hydrochloric acid, glycerin, and aromatic elixir.

Elixir Pepsini, Bismuthi, et Strychninæ (*Elixir of Pepsin, Bismuth, and Strychnine*).—A solution of strychnine and tartaric acid in elixir of pepsin and bismuth.

Elixir Pepsini et Bismuthi (*Elixir of Pepsin and Bismuth*).—A solution of pepsin in water and glycerin, mixed with glycerite of bismuth and aromatic elixir, and colored with tincture of caramel.

Elixir Pepsini et Ferri (*Elixir of Pepsin and Iron*).—A mixture of tincture of citro-chloride of iron and elixir of pepsin.

Elixir Pepsini at Rennini Compositum, Essentia Pepsini (*Compound Elixir of Pepsin and Rennin, Essence of Pepsin*).—A solution of pepsin and rennin in a mixture of lactic acid, glycerin and water, to which are added tincture of sweet orange peel and an alcoholic solution of oil of nutmeg. The required volume having been made up by the addition of water, purified talc is added, the mixture set aside for twenty-four hours with occasional agitation, and then filtered.

Elixir Phosphori (*Elixir of Phosphorus*).—A mixture of a chloroform solution of phosphorus with alcohol, glycerin, oil of anise, compound spirit of orange and water, filtered clear with the aid of purified talc.

Elixir Phosphori et Nucis Vomicæ (*Elixir of Phosphorus and Nux Vomica*).—A mixture of tincture of nux vomica and elixir of phosphorus.

Elixir Potassii Acetatis (*Elixir of Potassium Acetate*).—A solution of potassium acetate in aromatic elixir.

Elixir Potassii Acetatis et Juniperi (*Elixir of Potassium Acetate and Juniper*).—A mixture of fluidextract of juniper, potassium acetate, and aromatic elixir, to which purified talc has been added, and which is filtered after standing for twelve hours.

Elixir Potassii Bromidi (*Elixir of Potassium Bromide*).—A solution of potassium bromide in a mixture of water, syrup and aromatic elixir. It is usually colored by addition of compound tincture of cudbear in place of a like amount of aromatic elixir.

Elixir Quininæ Valeratis et Strychninæ (*Elixir of Quinine Valerate and Strychnine*).—A solution of quinine valerate and strychnine sulphate in aromatic elixir, colored with compound tincture of cudbear.

Elixir Rubi Compositum (*Compound Elixir of Blackberry*).—A mixture of a diluted alcohol tincture of blackberry root, nutgall, Saigon cinnamon, cloves, mace, and ginger with blackberry syrup, which is allowed to stand for several days and then filtered.

Elixir Sodii Bromidi (*Elixir of Sodium Bromide*).—A solution of sodium bromide in a mixture of syrup, water, and aromatic elixir.

Elixir Sodii Hypophosphitis (*Elixir of Sodium Hypophosphite*).—A solution of sodium hypophosphite and hypophosphorous acid in aromatic elixir.

Elixir Sodii Salicylatis (*Elixir of Sodium Salicylate*).—A solution of sodium salicylate in a mixture of syrup, water, and aromatic elixir.

Elixir Sodii Salicylatis Compositum (*Compound Elixir of Sodium Salicylate*).—A mixture of a solution of sodium salicylate and potassium iodide in aromatic elixir with fluidextract of cimicifuga and fluidextract of gelsemium, filtered clear with the aid of purified talc.

Elixir Strychninæ Valeratis (*Elixir of Strychnine Valerate*).—A solution of strychnine valerate in aromatic elixir, flavored with tincture of vanilla and colored with compound tincture of cudbear.

Elixir Taraxaci Compositum (*Compound Elixir of Taraxacum*).—A mixture of the fluidextracts of taraxacum, wild cherry, and licorice, tincture of sweet orange peel, tincture of cinnamon, compound tincture of cardamom, and aromatic elixir. It is allowed to stand twelve hours and then filtered. This elixir does not keep well, being prone to precipitate, and requires repeated filtration. It possesses little medicinal value, and is used chiefly as a vehicle for quinine and similar substances.

Elixir Terpini Hydratis (*Elixir of Terpin Hydrate*).—A solution of terpin hydrate in alcohol, mixed with tincture of sweet orange peel, spirit of bitter almond, glycerin, syrup, and water.

Elixir Terpini Hydratis et Codeinæ (*Elixir of Terpin Hydrate and Codeine*).—A solution of codeine in elixir of terpin hydrate.

Elixir Terpini Hydratis et Diacetylmorphinæ, Elixir Terpini Hydratis cum Heroina (*Elixir of Terpin Hydrate and Diacetylmorphine, Elixir of Terpin Hydrate with Heroine*).—A solution of diacetylmorphine hydrochloride in elixir of terpin hydrate.

Elixir Trium Bromidorum (*Elixir of Three Bromides*).—A solution of the bromides of ammonium, potassium and sodium in compound elixir of almond, colored with cudbear.

Elixir Vanillini Compositum (*Compound Elixir of Vanillin*).—A mixture of compound spirit of vanillin, alcohol, glycerin, syrup and water, colored with tincture of caramel.

Elixir Viburni Opuli Compositum (*Compound Elixir of Viburnum Opulus, Compound Elixir of Crampbark*).—A mixture of the fluidextracts of viburnum opulus, aletris, and trillium with compound elixir of taraxacum. It is allowed to stand during twelve hours and filtered.

Elixir Viburni Prunifolii (*Elixir of Viburnum Prunifolium, Elixir of Black Haw*).—A mixture of fluidextract of viburnum prunifolium, compound tincture of cardamom, and aromatic elixir, which is allowed to stand during twelve hours and filtered.

Elixir Zinci Valeratis (*Elixir of Zinc Valerate*).—A solution of zinc valerate in a mixture of ammonium citrate, aromatic elixir and alcohol, which is flavored with spirit of bitter almond and colored with compound tincture of cudbear.

CHAPTER XIX.

SPIRITS OR ESSENCES.

IN the Pharmacopœia and *National Formulary* the term "spiritus" is used to designate an alcoholic solution of valatile substances, chiefly volatile oils; in a few cases water also is added. Of the 23 spirits recognized, all but 2 can be conveniently prepared by the pharmacist, as they are quickly made and require only the ordinary apparatus usually found in a drugstore; as a rule, they are prepared by simple solution of the liquid or gaseous body in alcohol, although sometimes resort is had to distillation. Whenever volatile oils are used in the preparation of spirits, only the very best should be selected, as the value of the finished product depends entirely upon the quality of the oil; particular attention should be paid to those oils likely to have acquired a terebinthinate odor, sucn as the oils of juniper, lemon, nutmeg, and orange peel.

The following is a list of the official spirits, together with their composition:

Latin name.	English name.	Composition.
Spiritus Acidi Formici Nat. Form.	Spirit of Formic Acid (Spirit of Ants) . . .	A solution of formic acid in water and alcohol. This preparation is practically identical with Spiritus Formicarum of the German Pharmacopœia.
Spiritus Ætheris . . U. S. P.	Spirit of Ether .	A solution of ether 3¼ volumes in alcohol 6¾ volumes. This spirit is usually designated by Germans as Hoffmann's Drops.
Spiritus Ætheris Compositus . . . . Nat. Form.	Compound Spirit of Ether (Hoffman's Anodyne)	A mixture of ethereal oil, 2.5 volumes; ether, 32.5 volumes, and alcohol, 65 volumes.
Spiritus Ætheris Nitrosi . . . . . U. S. P.	Spirit of Nitrous Ether . . .	An alcoholic solution of ethyl nitrite, containing, when freshly made, between 4 and 5 per cent. of the ester. This spirit is popularly known as Sweet Spirit of Nitre.
Spiritus Ammoniæ Anisatus . . . . Nat. Form.	Anisated Spirit of Ammonia . .	A solution of anethol in alcohol, with the addition of ammonia water.
Spiritus Ammoniæ Aromaticus . . . . U. S. P.	Aromatic Spirit of Ammonia . .	A hydroalcoholic solution of normal ammonium carbonate, containing 70 per cent. by volume of alcohol, 1 per cent. of oil of lemon, and $\frac{1}{10}$ per cent. each of oil of lavender flowers and oil of nutmeg.
Spiritus Amygdalæ Amaræ . . . . . U. S. P.	Spirit of Bitter Almond . . .	A hydroalcoholic solution of oil of bitter almond, containing 1 per cent. by volume of the oil.
Spiritus Anisi . . U. S. P.	Spirit of Anise .	A 10 per cent. by volume solution of oil of anise in alcohol.

Latin name.	English name.	Composition.
Spiritus Aurantii Compositus . . . . U. S. P.	Compound Spirit of Orange .	A solution of oil of orange 20 volumes, oil of lemon 5 volumes, oil of coriander 2 volumes, oil of anise ½ volume in alcohol 72½ volumes.
Spiritus Camphoræ . U. S. P.	Spirit of Camphor	A solution of camphor, 100 Gms., in sufficient alcohol to make 1000 mils. (or Cc.) of spirit.
Spiritus Cardamomi Compositus . . Nat. Form.	Compound Spirit of Cardamom.	A solution of anethol and the oils of cardamom, orange, cinnamon, clove and caraway in alcohol.
Spiritus Chloroformi U. S. P.	Spirit of Chloroform . . .	A 6 per cent. by volume solution of chloroform in alcohol.
Spiritus Cinnamomi . U. S. P.	Spirit of Cinnamon . . .	A 10 per cent. by volume solution of oil of cinnamon in alcohol.
Spiritus Glycerylis Nitratis . . . . U. S. P.	Spirit of Glyceryl Trinitrate .	A 1 per cent. by weight solution of glyceryl trinitrate in alcohol.
Spiritus Juniperi . . U. S. P.	Spirit of Juniper	A 5 per cent. by volume solution of oil of juniper in alcohol.
Spiritus Juniperi Compositus . . . . U. S. P.	Compound Spirit of Juniper .	A hydroalcoholic solution containing 0.4 per cent. by volume of oil of juniper, 0.05 per cent. by volume each of the oils of fennel and caraway, and 70 per cent. by volume of alcohol
Spiritus Lavandulæ . U. S. P.	Spirit of Lavender	A 5 per cent. by volume solution of oil of lavender in alcohol.
Spiritus Menthæ Piperitæ. . . . . U. S. P.	Spirit of Peppermint . . .	A 10 per cent. by volume solution of oil of peppermint in alcohol, colored green with peppermint herb. This spirit is popularly called Essence of Peppermint.
Spiritus Menthæ Viridis . . . . . U. S. P.	Spirit of Spearmint . . .	A 10 per cent. by volume solution of oil of spearmint in alcohol, colored green with spearmint herb. This spirit is often called Essence of Spearmint.
Spiritus Myrciæ Compositus . . . . Nat. Form.	Compound Spirit of Myrcia .	A solution of the oils of myrcia, orange and pimenta in alcohol, with the addition of water.
Spiritus Odoratus . Nat. Form.	Perfumed Spirit.	A solution of acetic ether and the oils of bergamot, lemon, rosemary, lavender and orange flowers in alcohol, with the addition of water.
Spiritus Sinapis . . Nat. Form.	Spirit of Mustard	A solution of volatile oil of mustard in alcohol.
Spiritus Vanillini Compositus . . . . Nat. Form.	Compound Spirit of Vanillin .	A solution of vanillin and the oils of orange, cardamom and cinnamon in alcohol.

SPECIAL REMARKS.

Spiritus Ætheris Nitrosi.—Spirit of nitrous ether, popularly better known as Sweet Spirit of Nitre, is a rather unstable solution, at least as far as the proportion of active ingredient is concerned; even under favorable conditions it deteriorates; to retard this change as far as possible, the spirit should be preserved in small, well stoppered bottles, in a cool, dark place. Spirit of nitrous ether should be purchased in original packages, and never in bulk drawn from carboys.

The chemical reactions involved in the manufacture of this spirit will be explained elsewhere, as also the official method of determining its quality.

Spiritus Ammoniæ Aromaticus.—Ammonia water is used in connection with official ammonium carbonate, for the purpose of converting the latter into the normal salt, as this alone is soluble in the alcoholic liquid; in order to complete the change, it is advisable to let the aqueous solution stand for twelve or twenty-four hours before adding to it the mixture of oils and alcohol. Aromatic spirit of ammonia is of faint color when freshly prepared, but gradually becomes darker.

Spiritus Amygdalæ.—The official spirit of bitter almond is intended for medicinal purposes and should not be sold as Essence or Extract of Bitter Almond for flavoring purposes, on account of the presence of hydrocyanic acid. The flavoring essence or extract should be made from synthetic oil of bitter almond, which contains no hydrocyanic acid and is officially designated as benzaldehyde.

Spiritus Camphoræ (*Spirit of Camphor*).—Although the preparation of this solution presents no difficulty whatever and requires but ordinary care in weighing and measuring, commercial spirit of camphor has at times been found deficient in camphor to the extent of 25 to 30 per cent.; added water has also been found present. Both conditions point to wilful adulteration and are violations of the Federal and State drug laws.

The Pharmacopœia requires that spirit of camphor, when assayed, shall yield not less than 9.5 Gms. nor more than 10.5 Gms. of camphor in every 100 mils. (or Cc.); the presence of added water is officially determined by adding to 5 mils. (or Cc.) of spirit of camphor 0.050 Gm. of anhydrous potassium carbonate, when the latter should neither liquefy nor adhere to the bottom of the vessel.

Spiritus Glycerylis Nitratis.—Spirit of glyceryl trinitrate was formerly officially recognized as spirit of glonoin, a name originally given to the preparation by the homœopaths. It is also sometimes called spirit of nitroglycerin and spirit of trinitrin, but these names are improper and should not be used. The spirit should be transported in well stoppered tin cans and kept in a cool place remote from light and fire. If through accident some of the spirit be spilled, especially a large quantity, a solution of potassium hydoxide should be at once poured over it to effect decomposition, and thus avert the danger which would arise from evaporation of the alcohol and leaving the explosive glyceryl trinitrate as a residue.

CHAPTER XX.

TINCTURES.

TINCTURE is the name applied to solutions of non-volatile or only partially volatile substances, in liquids other than simple water or glycerin, and which invariably contain alcohol; solutions of volatile substances in alcohol are always termed spirits or essences. While tinctures are usually assumed to be solutions of vegetable principles, this is not the case in all the official tinctures; two of these, the tinctures of iodine and of ferric chloride, are solutions of inorganic substances, and must also be classed as exceptions to the rule that tinctures are solutions of non-volatile substances. The menstruum or solvent used in the preparation of tinctures may be simply alcohol, various mixtures of alcohol and water, or of alcohol, glycerin, and water, ammoniated alcohol in the form of aromatic spirit of ammonia, and mixtures of alcohol and ether; according as these different menstrua are employed, tinctures are dividedin to groups designated as alcoholic, hydroalcoholic, ammoniated, and ethereal tinctures, respectively. Ethereal tinctures are not recognized in the U. S. Pharmacopœia, but a general formula for their preparation is given in the *National Formulary;* they are used to some extent in Europe and may be found in some of the foreign pharmacopœias.

The Pharmacopœia recognizes 54 tinctures, of which 15 are made with alcohol, 36 with mixtures of alcohol and water and in some cases the addition of glycerin, 1 with water and subsequent addition of alcohol, and 2 with aromatic spirit of ammonia; of the 49 tinctures of the *National Formulary*, 8 are made with alcohol, 37 with mixtures of alcohol and water, 2 with mixtures of alcohol and ether, and 1 each with an ammoniacal mixture of alcohol and water, and boiling water. From this it is seen that the tendency is in the direction of weaker alcohol, and many tinctures formerly made with alcohol exclusively are now found equally efficient and permanent when made with a mixture of alcohol and water. The valuable solvent and preservative properties of alcohol have been explained in a preceding chapter; these are retained in the various hydroalcoholic mixtures, in which the proportions of alcohol and water are so adjusted that complete extraction of the valuable constituents of the drug is insured as well as permanence of the solution; the solution of much inert and unstable matter is likewise thus avoided. Tinctures made with weak alcohol are also more readily miscible with aqueous liquids—a point often of great value in dispensing medicines. The addition of glycerin to the menstruum is frequently desirable to facilitate the perfect extraction

of astringent and other principles, and to prevent subsequent changes in the finished tincture, due to atmospheric influences, which cause gelatinization of the solution or deposit of unsightly precipitates.

The following is a list of the tinctures containing glycerin. Tinctures of the U. S. Pharmacopœia: camphorated tincture of opium, 4 per cent.; compound tincture of cardamom, 5 per cent.; tincture of cinchona, 7.5 per cent.; compound tincture of cinchona, 7.5 per cent.; tincture of cinnamon, 7.5 per cent.; compound tincture of gentian, 10 per cent.; tincture of lactucarium, 25 per cent.; tincture of rhubarb, 10 per cent.; aromatic tincture of rhubarb, 10 per cent. Tinctures of the *National Formulary:* bitter tincture of zedoary, 12.5 per cent.; sweet tincture of rhubarb, 10 per cent.; compound tincture of viburnum, 7.5 per cent.; tincture of nutgall, 10 per cent.

Tinctures are, as a rule, prepared by percolation, except in the case of balsams, gum-resins, resins, and extractive drugs, for which maceration is decidedly preferable, either because the drug cannot be reduced conveniently to a uniform powder suitable for percolation, as in the case of asafetida, benzoin, myrrh, etc., or because solution takes place too rapidly, causing impaction of the mass in the percolator, as in the case of gambir, guaiac, etc. The process of percolation has been fully described on page 143 *et seq.*, as well as the precautions necessary to insure perfect extraction of drugs. The great advantages to be derived from a proper moistening and preliminary maceration of the drug have been pointed out in the chapter on Percolation. The value of this mode of solution cannot be overestimated in the preparation of tinctures, and as the amount of available menstruum is ample, complete exhaustion of the drug will have been effected before all the solvent has passed through; the objection urged that menstruum is retained by the marc can be easily overcome (see page 149), and is but trifling as compared with the gain in time and in the perfect, clear solution at once obtained.

In the case of tinctures to be made by percolation, the Pharmacopœia, with a few exceptions (the tinctures of arnica, cantharides, lactucarium, opium, deodorized opium, squill, and strophanthus), directs that the powdered drug or mixture of drugs be moistened with a sufficient quantity of the prescribed menstruum to render it evenly and distinctly damp; it is then transferred to a percolator, and, without pressing the powder, allowed to stand for six hours, the percolator being well covered to prevent loss of alcohol. The drug is then packed firmly, unless otherwise directed, and sufficient menstruum is poured on to saturate the powder and leave a stratum above it; when the liquid begins to drop from the percolator, the lower orifice is closed, the percolator closely covered, and the drug allowed to macerate for twenty-four hours. Finally percolation is allowed to proceed slowly, menstruum being gradually poured on top of the drug, until the required volume of tincture has been collected.

The preliminary treatment is intended to insure more thorough

penetration of the cellular tissue by the menstruum, and has been found very effectual in furthering the extraction of the soluble principles sought.

The rate of flow for tinctures made by percolation should not exceed 15 or 20 drops per minute, and in the case of the tinctures of aconite, cinchona and nux vomica should be reduced to 10 drops.

In the case of tinctures to be standardized by assay, percolation is allowed to proceed until 95 per cent. of the proposed volume of percolate has been collected; the latter having been thoroughly mixed, a portion is assayed according to the official directions given under the respective tinctures, and, having calculated from the results obtained the amount of alkaloids in the remainder of the percolate, sufficient menstruum is added to make the finished product conform to the prescribed alkaloidal standard.

When tinctures are to be made by maceration, the Pharmacopœia directs that three-fourths of the total prescribed menstruum be added to the powdered drug or mixture of drugs (unless a different quantity is specified in the official formula), and the mixture set aside in a tightly stoppered bottle or flask, in a moderately warm place, with frequent agitation, for a period of three days (or longer if necessary). The mixture is then transferred to a plain filter and allowed to drain, the residue on the filter being washed with sufficient menstruum, gradually added, to bring the filtrate up to the required volume.

The funnel should be kept closely covered during filtration to avoid loss of alcohol. Since the paper filter will absorb considerable liquid it will be found more convenient in the majority of cases to filter the mixture through a pledget of absorbent cotton pressed into the throat of the funnel; this plan also facilitates washing of the residue in the funnel.

The directions of the *National Formulary* for the preparation of tinctures by percolation and maceration are practically identical with those of the Pharmacopœia, except that the time specified for maceration has been fixed at seven days.

Of the 103 tinctures of the Pharmacopœia and the *National Formulary*, 67, or about two-thirds of the whole number, are directed to be made by percolation, 22 by maceration, 13 by direct solution, and 1 by decoction and subsequent concentration.

In the pharmacopœial titles of tinctures, the names of the drugs furnishing the active ingredients are indicated in all but 10; of these, 6 are designated as *compound tinctures*, namely: the *compound tinctures* of *benzoin, cardamom, cinchona, gambir, gentian,* and *lavender.* In the remaining 4 titles only the name of the chief ingredient is mentioned, as *tinctures of aloes, camphorated tincture of opium, tincture of rhubarb,* and *aromatic tincture of rhubarb.* In the *National Formulary's* titles of tinctures a similar arrangement prevails; in 30 the name of the chief active ingredient is mentioned, 5 are designated as compound tinctures, in 6 a distinctive name has been selected without reference to any

medicinal ingredient present, and in 8 the name of the chief active constituent has been qualified by addition of a special adjective.

Upon exposure to air and light, tinctures, like all vegetable solutions, are prone to undergo change, and should, therefore, be kept in well closed containers, in places not exposed to direct sunlight; extremes of temperature are equally hurtful on account of possible change in the menstruum. Fortunately, the deposits formed in tinctures consist, as a rule, only of inert extractive matter, which may be removed by filtration.

The following table shows the composition and strength of the official tinctures, as well as the fineness of powder and the menstruum used in their preparation.

TABLE OF U. S. P. TINCTURES ARRANGED ALPHABETICALLY.

Made by Direct Solution.

Latin name.	English name.	Mode of preparation.
Tinctura Ferri Chloridi	Tincture of Ferric Chloride	Made by mixing 350 mils. (or Cc.) of solution of ferric chloride with sufficient alcohol to produce 1000 mils. (or Cc.) of tincture, and setting the liquid aside in an amber-colored bottle for at least 3 months before dispensing.
Tinctura Iodi	Tincture of Iodine	Made by dissolving 50 Gms. of potassium iodide in 50 mils. (or Cc.) of distilled water, adding to this solution 70 Gms. of iodine and agitating the mixture until the iodine is completely dissolved, and finally adding sufficient alcohol to produce 1000 mils. (or Cc.) of tincture.

Made by Maceration.

Tinctura Aloes	Tincture of Aloes	Made by macerating 100 Gms. of aloes and 200 Gms. of licorice root, both in No. 40 powder, with diluted alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Asafœtidæ	Tincture of Asafetida	Made by macerating 200 Gms. of asafetida, bruised, with alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Aurantii Dulcis	Tincture of Sweet Orange Peel	Made by macerating 500 Gms. of sweet orange peel, grated from the fresh fruit, with alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Benzoini	Tincture of Benzoin	Made by macerating 200 Gms. of benzoin, in No. 40 powder, with alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Benzoini Composita	Compound Tincture of Benzoin	Made by macerating 100 Gms. of benzoin and 20 Gms. of aloes, both in No. 40 powder, together with 80 Gms. of storax and 40 Gms. of balsam of tolu, with alcohol, to make 1000 mils. (or Cc.) of tincture.

Latin name.	English name.	Mode of preparation.
Tinctura Cardamomi Composita	Compound Tincture of Cardamom	Made by macerating 20 Gms. of cardamom seed and 12 Gms. of caraway, both in No. 40 powder, together with 25 Gms. of Saigon cinnamon and 5 Gms. of cochineal, both in No. 60 powder, with a mixture of glycerin 50 volumes and diluted alcohol 950 volumes., to make 1000 mils. (or Cc.) of tincture.
Tinctura Gambir Composita	Compound Tincture of Gambir (Compound Tincture of Pale Catechu)	Made by macerating 50 Gms. of gambir and 25 Gms. of Saigon cinnamon, both in No. 50 powder, with diluted alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Guaiaci	Tincture of Guaiac	Made by macerating 200 Gms. of guaiac, in No. 40 powder, with alcohol to make 1000 mils. (or Cc.) of tincture.
Tinctura Guaiaci Ammoniata	Ammoniated Tincture of Guaiac	Made by macerating 200 Gms. of guaiac, in No. 40 powder, with aromatic spirit of ammonia, to make 1000 mils. (or Cc.) of tincture.
Tinctura Kino	Tincture of Kino	Made by digesting 100 Gms. of kino with hot water on a waterbath for 1 hour; when cool, boiled water is added and then an equal volume of alcohol, and the mixture macerated for 24 hours, to make 1000 mils. (or Cc.) of tincture.
Tinctura Lavandulæ Composita	Compound Tincture of Lavender (Compound Spirit of Lavender)	Made by macerating 20 Gms. of Saigon cinnamon, 5 Gms. of cloves, and 10 Gms. each of nutmeg and red saunders, all in No. 50 powder, with a solution of 8 mils. of oil of lavender and 2 mils. of oil of rosemary in a mixture of 750 mils. (or Cc.) of alcohol and 250 mils. (or Cc.) of water.
Tinctura Limonis Corticis	Tincture of Lemon Peel	Made by macerating 500 Gms. of lemon peel, grated from the fresh fruit, with alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Moschi	Tincture of Musk	Made by macerating 5 Gms. of musk with 45 mils. (or Cc.) of water for 24 hours then adding 45 mils. (or Cc.) of alcohol and macerating again for 6 days; finally filtering and washing the residue with diluted alcohol to make 100 mils. (or Cc.) of tincture.
Tinctura Myrrhæ	Tincture of Myrrh	Made by macerating 200 Gms. of myrrh, in moderately coarse powder, with alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Opii Camphorata	Camphorated Tincture of Opium (Paregoric)	Made by macerating 4 Gms. each of powdered opium, benzoic acid and camphor, and 4 mils. (or Cc.) of oil of anise, with a mixture of 40 mils. (or Cc.) of glycerin and 950 mils. (or Cc.) of diluted alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Tolutana	Tincture of Tolu	Made by macerating 200 Gms. of balsam of tolu with alcohol to make 1000 mils. (or Cc.) of tincture.

Made by Percolation.

Latin name.	English name.	Mode of preparation.
Tinctura Aconiti	Tincture of Aconite	Made by percolating 100 Gms. of aconite, in No. 40 powder, with a mixture of alcohol 7 volumes and water 3 volumes. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 0.05 Gm. of the ether-soluble alkaloids of aconite.
Tinctura Arnicæ	Tincture of Arnica	Made by percolating 200 Gms. of arnica, in No. 20 powder, with diluted alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Aurantii Amari	Tincture of Bitter Orange Peel	Made by percolating 200 Gms. of bitter orange peel, in No. 40 powder, with a mixture of alcohol 3 volumes and water 2 volumes, to make 1000 mils. (or Cc.) of tincture.
Tinctura Belladonnæ Foliorum	Tincture of Belladonna Leaves	Made by percolating 100 Gms. of belladonna leaves, in No. 60 powder, with diluted alcohol. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 0.03 Gm. of the total alkaloids of belladonna leaves.
Tinctura Calumbæ	Tincture of Calumba	Made by percolating 200 Gms. of calumba, in No. 20 powder, with a mixture of alcohol 3 volumes and water 2 volumes, to make 1000 mils. (or Cc.) of tincture.
Tinctura Cannabis	Tincture of Cannabis	Made by percolating 100 Gms. of cannabis, in No. 40 powder, with alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Cantharidis	Tincture of Cantharides	Made by digesting 100 Gms. of cantharides, in No. 60 powder, with alcohol for 24 hours at a temperature of from 50° to 55° C. with frequent agitation; then transfer to a percolator, allow the mixture to drain and percolate with sufficient alcohol to make 1000 mils. (or Cc.) of tincture.
Tinctura Capsici	Tincture of Capsicum	Made by percolating 100 Gms. of capsicum, in No. 50 powder, with a mixture of alcohol 95 volumes and water 5 volumes, to make 1000 mils. (or Cc.) of tincture.
Tinctura Cardamomi	Tincture of Cardamom	Made by percolating 150 Gms. of cardamom seed, in No. 40 powder, diluted alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Cinchonæ	Tincture of Cinchona	Made by percolating 200 Gms. of cinchona, in No. 40 powder, with a mixture of glycerin 75 mils. (or Cc.), alcohol 675 mils. (or Cc.) and water 250 mils. (or Cc.), followed by a mixture of alcohol 2 volumes and water 1 volume. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 0.5 Gm. of the total alkaloids of cinchona.

Latin name.	English name.	Mode of preparation.
Tinctura Cinchonæ Composita	Compound Tincture of Cinchona	Made by percolating 100 Gms. of red cinchona and 80 Gms. of bitter orange peel, both in No. 40 powder, and 20 Gms. of serpentaria, in No. 60 powder, with a mixture of glycerin 75 mils. (or Cc.), alcohol 675 mils. (or Cc.) and water 250 mils. (or Cc.), followed by a mixture of alcohol 2 volumes and water 1 volume. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 0.5 Gm. of the total alkaloids of cinchona.
Tinctura Cinnamomi	Tincture of Cinnamon	Made by percolating 200 Gms. of Saigon cinnamon, in No. 50 powder, with a mixture of glycerin 75 volumes, alcohol 675 volumes and water 250 volumes, to make 1000 mils. (or Cc.) of tincture.
Tinctura Colchici Seminis	Tincture of Colchicum Seed	Made by percolating 100 Gms. of colchicum seed, in No. 50 powder, with a mixture of alcohol 3 volumes and water 2 volumes. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 0.04 Gm. of colchicine.
Tinctura Digitalis	Tincture of Digitalis	Made by percolating 100 Gms. of digitalis, in No. 60 powder, with a mixture of alcohol 3 volumes and water 1 volume, to make 1000 mils. (or Cc.) of tincture.
Tinctura Gelsemii	Tincture of Gelsemium	Made by percolating 100 Gms. of gelsemium, in No. 60 powder, with a mixture of alcohol 65 volumes and water 35 volumes, to make 1000 mils. (or Cc.) of tincture.
Tinctura Gentianæ Composita	Compound Tincture of Gentian	Made by percolating 100 Gms. of gentian, 40 Gms. of bitter orange peel and 10 Gms. of cardamom seed, all in No. 40 powder, with a mixture of glycerin 100 mils. (or Cc.), alcohol 500 mils. (or Cc.) and water 400 mils. (or Cc.), to make 1000 mils. (or Cc.) of tincture.
Tinctura Hydrastis	Tincture of Hydrastis (Tincture of Golden Seal)	Made by percolating 200 Gms. of hydrastis, in No. 60 powder, with a mixture of alcohol 2 volumes and water 1 volume. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 0.4 Gm. of the ether-soluble alkaloids of hydrastis.
Tinctura Hyoscyami	Tincture of Hyoscyamus (Tincture of Henbane)	Made by percolating 100 Gms. of hyoscyamus, in No. 60 powder, with diluted alcohol. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 0.0065 Gm. of the total alkaloids of hyoscyamus.

Latin name.	English name.	Mode of preparation.
Tinctura Lactucarii	Tincture of Lactucarium	Made by first treating 500 Gms. of lactucarium beaten to a coarse powder with clean sand, twice with purified petroleum benzin, and after drying thoroughy percolating with a mixture of glycerin 250 mils. (or Cc.), water 250 mils. (or Cc.) and alcohol 500 mils. (or Cc.), followed by diluted alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Lobeliæ	Tincture of Lobelia	Made by percolating 100 Gms. of lobelia, in No. 50 powder, with diluted alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Nucis Vomicæ	Tincture of Nux Vomica	Made by percolating 100 Gms. of nux vomica, in No. 40 powder, with a mixture of alcohol 3 volumes and water 1 volume. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 0.25 Gm. of the total alkaloids of nux vomica.
Tinctura Opii	Tincture of Opium	Made by macerating 100 Gms. of granulated opium with water for 24 hours, then adding an equal volume of alcohol, again macerating for 48 hours with occasional agitation; the mixture is then percolated, diluted alcohol being gradually added until 950 mils. (or Cc.) of percolate is obtained. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 1 Gm. of anhydrous morphine.
Tinctura Opii Deodorati	Tincture of Deodorized Opium	Made by first macerating 100 Gms. of granulated opium with hot water for 24 hours and then percolating to exhaustion with water. After concentration of the liquid, it is treated twice with purified petroleum benzin, diluted with water and filtered; after adding 200 mils. (or Cc.) of alcohol to the filtrate, sufficient water is passed through the filter to bring the volume up to 950 mils (or Cc.). The liquid is assayed and adjusted to contain in 100 mils. (or Cc.) 1 Gm. of anhydrous morphine.
Tinctura Physostigmatis	Tincture of Physostigma (Tincture of Calabar Bean)	Made by percolating 100 Gms. of physostigma, in No. 50 powder with alcohol. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 0.015 Gm. of the alkaloids of physostigma.
Tinctura Pyrethri	Tincture of Pyrethrum (Tincture of Pellitory)	Made by percolating 200 Gms. of pyrethrum, in No. 50 powder, with alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Quassiæ	Tincture of Quassia	Made by percolating 200 Gms. of quassia, in No. 50 powder, with a mixture of alcohol 1 volume and water 2 volumes, to make 1000 mils. (or Cc.) of tincture.

Latin name.	English name.	Mode of preparation.
Tinctura Rhei	Tincture of Rhubarb	Made by percolating 200 Gms. of rhubarb and 30 Gms. of cardamom seed, both in No. 40 powder, with a mixture of glycerin 100 mils. (or Cc.), alcohol 500 mils. (or Cc.) and water 400 mils. (or Cc.), followed by diluted alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Rhei Aromatica	Aromatic Tincture of Rhubarb	Made by percolating 200 Gms. of rhubarb, 40 Gms. each of Saigon cinnamon and cloves, and 20 Gms. of nutmeg, all in No. 40 powder, with a mixture of glycerin 100 mils. (or Cc.), alcohol 500 mils. (or Cc.) and water 400 mils. (or Cc.), followed by diluted alcohol, to make 1000 mils. (or Cc.) of tincture.
Tinctura Sanguinariæ	Tincture of Sanguinaria (Tincture of Bloodroot)	Made by percolating 100 Gms. of sanguinaria, in No. 60 powder, with a mixture of alcohol 3 volumes and water 2 volumes acidulated with hydrochloric acid, followed by a mixture of alcohol and water made in the same proportions, to make 1000 mils. (or Cc.) of tincture.
Tinctura Scillæ	Tincture of Squill	Made by first macerating 100 Gms. of squill, in No. 20 powder, with a mixture of alcohol 3 volumes and water 1 volume for 24 hours in a moderately warm place, and then percolating slowly with the same menstruum, to make 1000 mils. (or Cc.) of tincture.
Tinctura Stramonii	Tincture of Stramonium	Made by percolating 100 Gms. of stramonium, in No. 60 powder, with diluted alcohol. The percolate is assayed and adjusted to contain in 100 mils. (or Cc.) 0.025 Gm. of the total alkaloids of the drug.
Tinctura Strophanthi	Tincture of Strophanthus	Made by first percolating 100 Gms. of strophanthus, in No. 40 powder, with sufficient purified petroleum benzin to remove all fatty matter, and then, after thoroughly drying the powder, percolating with alcohol, after 48 hours maceration, until 1000 mils. (or Cc.) of tincture are obtained.
Tinctura Tolutana	Tincture of Tolu	Made by macerating 200 Gms. of balsam of tolu with sufficient alcohol to produce 1000 mils. (or Cc.) of tincture.
Tinctura Valerianæ	Tincture of Valerian	Made by percolating 200 Gms. of valerian, in No. 40 powder, with a mixture of alcohol 3 volumes and water 1 volume, to produce 1000 mils. (or Cc.) of tincture.
Tinctura Valerianæ Ammoniata	Ammoniated Tincture of Valerian	Made by percolating 200 Gms. of valerian, in No. 40 powder, with aromatic spirit of ammonia, to produce 1000 mils. (or Cc.) of tincture.

Latin name.	English name.	Mode of preparation.
Tinctura Veratri Viridis	Tincture of Veratrum Viride	Made by percolating 100 Gms. of veratrum viride, in No. 60 powder, with alcohol, to produce 1000 mils. (or Cc.) of tincture.
Tinctura Zingiberis	Tincture of Ginger	Made by percolating 200 Gms. of Jamaica ginger, in No. 30 powder, with alcohol, to produce 1000 mils. (or Cc.) of tincture.

TABLE OF NAT. FORM. TINCTURES ARRANGED ALPHABETICALLY.

Made by Decoction.

Latin name.	English name.	Composition.
Tinctura Quillajæ	Tincture of Quillaja (Tincture of Soapbark)	Made by boiling quillaja, in No. 20 powder, with water for 15 minutes, straining while hot, washing the residue with boiling water and after the mixed liquids have become cool, adding alcohol and setting the mixture aside for 12 hours, and then filtering.

Made by Direct Solution.

Tinctura Caramelis	Tincture of Caramel	Made by dissolving caramel in water and adding alcohol as a preservative.
Tinctura Ferri Chloridi Ætherea	Ethereal Tincture of Ferric Chloride (Bestuscheff's Tincture, Lamotte's Drops)	Made by adding solution of ferric chloride to alcohol and adding ether, after which the liquid is exposed in flint glass bottles to the rays of the sun until completely decolorized. The bottles are then removed from the sunlight and occasionally opened until the liquid has again assumed a yellow color.
Tinctura Ferri Citro-Chloridi	Tincture of Ferric Citro-Chloride (Tasteless Tincture of Ferric Chloride, Tasteless Tincture of Iron)	Made by dissolving sodium citrate in a mixture of solution of ferric chloride and water with the aid of a gentle heat; alcohol is then added and when the liquid has become cold sufficient water to make up the required volume.
Tinctura Ferri Pomata (Tinctura Ferri Malatis Crudi)	Tincture of Ferrated Extract of Apples (Tincture of Crude Malate of Iron)	Made by dissolving ferrated extract of apples in cinnamon water and adding alcohol; after filtration, sufficient cinnamon water is added to make up the required volume.
Tinctura Guaiaci Composita	Compound Tincture of Guaiac (Dewees' Tincture of Guaiac)	Made by triturating guaiac, potassium carbonate, pimenta and pumice with alcohol, then adding water slowly and triturating the mixture thoroughly; finally the mixture is filtered and sufficient diluted alcohol added to make up the required volume.
Tinctura Iodi Fortior	Stronger Tincture of Iodine (Churchill's Tincture of Iodine)	Made by dissolving potassium iodide and iodine in water and adding alcohol to the solution.

Latin name.	English name.	Composition.
Tinctura Iodi Decolorata	Decolorized Tincture of Iodine	Made by digesting iodine, sodium thiosulphate and water, at a gentle heat, until complete solution is effected; alcohol is then added and afterward stronger ammonia water. When the liquid has become colorless, sufficient alcohol is added to make up the required volume.
Tinctura Ipecacuanhæ et Opii	Tincture of Ipecac and Opium (Tincture of Dover's Powder)	Made by adding fluidextract of ipecac to partially evaporated tincture of deodorized opium and after filtering, adding sufficient diluted alcohol to make up the required volume.
Tinctura Kino et Opii Composita (Tinctura Kino Composita)	Compound Tincture of Kino and Opium (Compound Tincture of Kino)	Made by triturating cochineal with aromatic spirit of ammonia and gradually adding diluted alcohol; tincture of kino, tincture of opium, spirit of camphor, and oil of clove are then added and finally sufficient diluted alcohol to make up the required volume.
Tinctura Pectoralis (Guttæ Pectorales)	Pectoral Tincture (Pectoral Drops, Bateman's Pectoral Drops)	Made by mixing tincture of opium, compound tincture of gambir, spirit of camphor, oil of anise, and caramel with sufficient diluted alcohol to make up the required volume.
	Made by Maceration.	
Tinctura Aloes et Myrrhæ	Tincture of Aloes and Myrrh	Made by macerating Socotrine aloes, myrrh, and glycyrrhiza, all in No. 40 powder, with a mixture of alcohol, 3 volumes, and water, 1 volume, for 7 days, with occasional agitation.
Tinctura Cacti Grandiflori	Tincture of Cactus Grandiflorus (Tincture of Night Blooming Cereus)	Made by first macerating cut and crushed cactus grandiflorus with alcohol for 7 days with occasional agitation; then express and set the liquid aside. Percolate the residue slowly with alcohol; mix the two fluids and filter.
Tinctura Gallæ	Tincture of Nutgall	Made by macerating nutgall, in No. 60 powder, with a mixture of glycerin and alcohol, for 7 days, with frequent agitation.
Tinctura Paracoto (Tinctura Coto)	Tincture of Paracoto	Made by macerating paracoto, finely bruised, in alcohol, for 7 days, decant the liquid, express the residue, and filter the united liquids.
Tinctura Persionis Composita	Compound Tincture of Cudbear	Made by macerating cudbear with a mixture of alcohol, 1 volume, and water, 2 volumes, for 12 hours; filter and add caramel previously dissolved in some of the same menstruum.
Tinctura Rhei Aquosa	Aqueous Tincture of Rhubarb	Made by macerating sliced rhubarb in a solution of potassium carbonate in water for 24 hours; after straining the mixture, the liquid is heated to the boiling point, alcohol and cinnamon water are added and the whole then filtered while still warm.

Made by Percolation.

Latin name.	English name.	Method of Preparation.
Tinctura Amara	Bitter Tincture (Stomaehic Tincture, Bitter Stomachic Drops, Stomach Drops)	Made by percolating a mixture of gentian, centaury, bitter orange peel, zedoary, all in No. 40 powder, with a menstruum composed of alcohol, 2 volumes, and water, 1 volume.
Tinctura Antiperiodica	Antiperiodic Tincture (Warburg's Tincture)	Made by percolating a mixture of rhubarb, angelica fruit, elecampane, saffron, fennel, gentian, zedoary, cubeb, agaric, pepper, Saigon cinnamon, Jamaica ginger, all in No. 30 powder, and myrrh and camphor, in coarse powder with a mixture of alcohol, 3 volumes, and water, 1 volume; in the percolate, extract of aloes and quinine bisulphate are dissolved with the aid of a gentle heat.
Tinctura Antiperiodica sine Aloe	Antiperiodic Tincture without Aloes (Warburg's Tincture without Aloes)	Made exactly like the preceding tincture, omitting the extract of aloes.
Tinctura Aromatica	Aromatic Tincture	Made by percolating a mixture of Saigon cinnamon, Jamaica ginger, and galangal, all in No. 40 powder, and cloves and cardamom seed, both in No. 20 powder, with a mixture of alcohol, 2 volumes, and water, 1 volume.
Tinctura Bryoniæ	Tincture of Bryonia	Made by percolating bryonia, in No. 40 powder, with alcohol.
Tinctura Calendulæ	Tincture of Calendula	Made by percolating calendula, in No. 20 powder, with alcohol.
Tinctura Capsici et Myrrhæ	Tincture of Capsicum and Myrrh (Hot Drops, Thomsonian Number Six)	Made by percolating a mixture of capsicum in No. 20 powder, myrrh, in coarse powder, and clean fine sand, with a mixture of alcohol, 9 volumes, and water, 1 volume.
Tinctura Cimicifugæ	Tincture of Cimicifuga	Made by percolating cimicifuga, in No. 40 powder, with alcohol.
Tinctura Cocculi Indici	Tincture of Cocculus Indicus (Tincture of Fish Berry)	Made by percolating cocculus indicus, in No. 30 powder, with diluted alcohol.
Tinctura Croci	Tincture of Saffron	Made by percolating saffron with diluted alcohol.
Tinctura Cubebæ	Tincture of Cubeb	Made by percolating cubeb, in No. 30 powder, with alcohol.
Tinctura Delphinii	Tincture of Larkspur	Made by percolating larkspur seed, in No. 30 powder, with alcohol.
Tinctura Ergotæ Ammoniata	Ammoniated Tincture of Ergot	Made by percolating ergot, in No. 20 powder, first with a mixture of ammonia water, alcohol and water, and then with a mixture of alcohol, 2 volumes, and water, 1 volume.
Tinctura Humuli	Tincture of Humulus (Tincture of Hops)	Made by percolating hops, in No. 40 powder, with diluted alcohol.

Latin name.	English name.	Method of preparation.
Tinctura Ignatiæ	Tincture of Ignatia	Made by percolating ignatia, in No. 60 powder, with a mixture of alcohol, 8 volumes, and water, 1 volume. The percolate is assayed and adjusted to contain 0.2 Gm. of total alkaloids of ignatia in every 100 milliliters.
Tinctura Jalapæ	Tincture of Jalap	Made by percolating jalap, in No. 60 powder, with a mixture of alcohol, 2 volumes, and water, 1 volume.
Tinctura Jalapæ Composita	Compound Tincture of Jalap	Made by percolating a mixture of jalap and scammony, both in No. 60 powder, with a menstruum composed of alcohol, 2 volumes, and water, 1 volume.
Tinctura Krameriæ	Tincture of Krameria	Made by percolating krameria, in No. 40 powder, with diluted alcohol.
Tinctura Opii Crocata	Tincture of Opium with Saffron	Made by macerating a mixture of granulated opium, saffron in No. 20 powder, Saigon cinnamon in No. 60 powder, and cloves in No. 30 powder, for 2 days with diluted alcohol, and then percolating. The percolate is assayed and adjusted to contain 1 Gm. of anhydrous morphine in every 100 milliliters.
Tinctura Passifloræ	Tincture of Passion Flower	Made by percolating passion flower, in No. 20 powder, with diluted alcohol.
Tinctura Persionis	Tincture of Cudbear	Made by percolating cudbear, in fine powder, with a mixture of alcohol, 3 volumes, and water, 1 volume.
Tinctura Pimpinellæ	Tincture of Pimpinella	Made by percolating pimpinella, in No. 40 powder, with a mixture of alcohol, 2 volumes, and water, 1 volume.
Tinctura Pulsatillæ	Tincture of Pulsatilla	Made by percolating pulsatilla, in No. 30 powder, with a mixture of alcohol, 3 volumes, and water, 1 volume.
Tinctura Rhei Dulcis	Sweet Tincture of Rhubarb	Made by percolating a mixture of rhubarb and glycyrrhiza, both in No. 40 powder, anise and cardamom seed, both in No. 20 powder, with a mixture of glycerin, alcohol and water, and afterward with diluted alcohol.
Tinctura Sabal et Santali	Tincture of Saw Palmetto and Santal	Made by first macerating sabal, in about No. 16 powder, and sandal wood, in No. 60 powder, for 2 days with a mixture of alcohol, 4 volumes, and water, 1 volume, and then percolating with the same menstruum.
Tinctura Serpentariæ	Tincture of Serpentaria	Made by percolating serpentaria, in No. 50 powder, with a mixture of alcohol, 2 volumes, and water, 1 volume.
Tinctura Sumbul	Tincture of Sumbul	Made by percolating sumbul, in No. 30 powder, with a mixture of alcohol, 65 volumes, and water, 35 volumes.

Latin name.	English name.	Method of preparation.
Tinctura Vanillæ	Tincture of Vanilla	Made by first macerating vanilla, cut into small pieces, with alcohol for 2 days frequently agitating; then filter, reserving the filtrate and drying the drug by exposure to the air. Having ground the dry residue with sugar to a uniform powder, percolate the same with a mixture of the above filtrate and an equal volume of water, finally using diluted alcohol to make up the required volume.
Tinctura Viburni Opuli Composita	Compound Tincture of Viburnum	Made by first macerating a mixture of viburnum opulus, dioscorea, scutellaria and Saigon cinnamon, all in No. 40 powder, and cloves, in No. 20 powder, for 48 hours with a mixture of glycerin, alcohol and water, and then percolate following with a mixture of alcohol, 2 volumes, and water, 1 volume.
Tinctura Zedoariæ Amara	Bitter Tincture of Zedoary	Made by percolating a mixture of zedoary, rhubarb, gentian and agaric, all in No. 40 powder, aloes, in fine powder, and saffron with a mixture of alcohol, 2 volumes, and water, 1 volume, collecting three-fourths of the intended final volume; add glycerin to the percolate and set aside. Continue percolation to exhaustion of the drugs, evaporate the last percolate, mix it with the reserved portion and add sufficient of the alcohol-water mixture to make up the required volume.

The strength of the tinctures of the U. S. Pharmacopœia varies from 1.6 to 50 Gms. of drug, being in the majority of cases 10 or 20 Gms. for every 100 mils. (or Cc.) of finished product. The strength of the official British tinctures varies from 12.5 Gms. to 250 Gms. in 1000 mils. (or Cc.); of the 71 tinctures recognized, 33 are directed to be made by percolation, 20 by maceration, 18 by direct solution. The French and German Pharmacopœias direct their tinctures to be prepared by maceration, and, almost without exception, of such strength that 1 part of the drug is represented by about 5 or 10 parts of tincture by weight.

The following table represents a classification of the official tinctures based upon the amount of drug represented in each liter:

TABLE OF U. S. P. TINCTURES ARRANGED ACCORDING TO STRENGTH.

0.065 Gm. of total alkaloids in 1000 mils. (or Cc.)	Tinctura Hyoscyami
0.150 Gm. of alkaloids in 1000 mils. (or Cc.)	" Physostigmatis
0.250 Gm. of total alkaloids in 1000 mils. (or Cc.)	" Stramonii
0.300 Gm. of total alkaloids in 1000 mils. (or Cc.)	" Belladonnæ Foliorum.
0.500 Gm. of ether-soluble alkaloids in 1000 mils. (or Cc.)	" Aconiti.
0.400 Gm. of colchicine in 1000 mils. (or Cc.)	" Colchici Seminis.
2.500 Gms. of total alkaloids in 1000 mils. (or Cc.)	" Nucis Vomicæ.
4.000 Gms. of ether-soluble alkaloids in 1000 mils. (or Cc.)	" Hydrastis.
5.000 Gms. of total alkaloids of cinchona in 1000 mils. (or Cc.)	" Cinchonæ Composita.
10.000 Gms. of total alkaloids in 1000 mils. (or Cc.)	" Cinchonæ.
10.000 Gms. of anhydrous morphine in 1000 mils. (or Cc.)	" Opii.
10.000 Gms. of anhydrous morphine in 1000 mils. (or Cc.)	" Opii Deodorati.

TABLE OF U. S. P. TINCTURES ARRANGED ACCORDING TO STRENGTH.—*Continued.*

16 Gms. of drug in 1000 mils. (or Cc.)	Tinctura Opii Camphorata.
50 Gms. of drug in 1000 mils. (or Cc.)	" Kino.
	" Moschi.
55 Gms. of drug in 1000 mils. (or Cc.)	" Lavandulæ Composita.
62 Gms. of drug in 1000 mils. (or Cc.)	" Cardamomi Composita.
75 Gms. of drug in 1000 mils. (or Cc.)	" Gambir Composita.
	" Cantharidis.
	" Cannabis.
	" Capsici.
	" Digitalis.
100 Gms. of drug in 1000 mils. (or Cc.)	" Gelsemii.
	" Lobeliæ.
	" Sanguinariæ.
	" Scillæ.
	" Strophanthi.
	" Veratri Viridis.
120 Gms. of drug in 1000 mils. (or Cc.)	" Iodi.
136 Gms. (about) of anhydrous salt in 1000 mils. (or Cc.)	" Ferri Chloridi.
150 Gms. of drug in 1000 mils. (or Cc.)	" Gentianæ Composita.
	" Cardamomi.
	" Arnicæ.
	" Asafœtidæ.
	" Aurantii Amari.
	" Benzoini.
	" Calumbæ.
	" Cinnamomi.
200 Gms. of drug in 1000 mils. (or Cc.)	" Guaiaci.
	" Guaiaci Ammoniata.
	" Myrrhæ.
	" Pyrethri.
	" Quassiæ.
	" Tolutana.
	" Valerianæ.
	" Valerianæ Ammoniata.
	" Zingiberis.
230 Gms. of drug in 1000 mils. (or Cc.)	" Rhei.
240 Gms. of drug in 1000 mils. (or Cc.)	" Benzoini Composita.
300 Gms. of drug in 1000 mils. (or Cc.)	" Aloes.
	" Rhei Aromatica.
500 Gms. of drug in 1000 mils. (or Cc.)	" Aurantii Dulcis.
	" Lactucarii.
	" Limonis Corticis.

SPECIAL REMARKS.

Tinctura Aconiti (*Tincture of Aconite*).—This important tincture requires care in its preparation, as the drug is not easily exhausted. The drug from which it is to be made should have been assayed and contain not less than 0.5 per cent. of ether-soluble alkaloids, and percolation must be conducted at a rate not exceeding 10 drops per minute. The tincture has a yellowish-brown color and becomes turbid if mixed with water, owing to the precipitation of resin.

The Pharmacopœia requires that 100 mils. (or Cc.) of tincture of aconite shall yield, when assayed, not less than 0.045 Gm. nor more than 0.055 Gm. of the ether-soluble alkaloids of the drug, which consist chiefly of aconitine. It also states that if assayed biologically, the minimum lethal dose should not be greater than 0.0004 mil. (or Cc.) for each gram of body weight of the guinea-pig.

Tinctura Aloes (*Tincture of Aloes*).—Although the Pharmacopœia directs this tincture to be prepared by maceration, it can be made as well by percolation, provided the mixture of drugs be not packed firmly. Tincture of aloes has a dark blackish-brown color, and the bitter taste of the aloes is materially modified by the licorice root.

Tinctura Arnicæ (*Tincture of Arnica*).—The directions of the present Pharmacopœia are a decided improvement on those of the last. In

the author's experience, a No. 30 powder is preferable to the coarser powder officially directed, and, for such quantities of tincture of arnica as the pharmacist is likely to make at one time (say 2 or 3 liters), firm packing with continuous slow percolation, limited to 10 drops per minute, will yield equally good results in less time than the interrupted percolation with repeated maceration ordered by the Pharmacopœia. The tincture has a yellowish-brown color and the characteristic odor of the flowers.

Tinctura Asafœtidæ (*Tincture of Asafetida*).—Since some of the commercial asafetida is of inferior quality, only select gum-resin, containing not less that 60 per cent. of matter soluble in alcohol should be used for making the tincture, the value of the drug residing in the resinous constituents. Tincture of asafetida has a brownish-red color and the disagreeable odor of the drug. When added to aqueous fluids it forms milky mixtures, owing to precipitation of resin.

Tinctura Aurantii Amari (*Tincture of Bitter Orange Peel*).—This tincture should not be confounded with the next following tincture. It is made by exhausting the rind of the unripe bitter orange with a hydroalcoholic menstruum, and has a greenish-brown color and a bitter taste.

Tinctura Aurantii Dulcis (*Tincture of Sweet Orange Peel*).—Only the fresh peel from sweet oranges should be used for this tincture, the outer rind, rich in oil cells, alone being used. The tincture has a deep reddish-yellow color and a strong fragrant odor, and is superior to a solution of oil of orange peel in alcohol as a flavoring agent. The tincture of orange of the British Pharmacopœia closely resembles this preparation in color and odor, but is made from the fresh peel of bitter oranges.

Tinctura Belladonnæ Foliorum (*Tincture of Belladonna Leaves*).—Owing the variation in alkaloidal content of commercial belladonna leaves, the tincture should be made from assayed leaves containing not less than 0.30 per cent. of alkaloids. If the official directions be followed, the drug is not difficult to exhaust, the resulting tincture having a greenish-brown color and a heavy narcotic odor. The Pharmacopœia requires that tincture of belladonna leaves, when assayed, shall yield not less than 0.027 Gm. nor more than 0.033 Gm. of the total alkaloids of the drug used, in every 100 mils. (or Cc.).

Tinctura Benzoini Composita (*Compound Tincture of Benzoin*).—This tincture is intended to take the place of numerous semiproprietary preparations formerly much used, such as Wade's, Vervain's, Saint Victor's, Jesuit's, Friars', Turlington's, Persian, and Swedish Balsam; it should, however, never be substituted for any of the latter preparations if called for by the public under their respective names. It is of a deep red-brown color, has a rather pleasant balsamic odor, and yields with water a reddish-white opaque mixture having an acid reaction.

Tinctura Cannabis (*Tincture of Cannabis*).—Since the Pharmacopœia recognizes both the American-grown and the Indian varieties

of hemp under the official title Cannabis, the name of the tincture has been changed. When physicians prescribe Tincture of Indian Cannabis, pharmacists should dispense a tincture made from the Indian hemp only, while the official title Tincture of Cannabis may be applied to a preparation made from either variety of the drug. The Pharmacopœia requires that tincture of cannabis shall be assayed biologically, and when administered to dogs shall produce incoördination in a dose of not more than 0.3 mil. (or Cc.) per kilogram of body weight.

The British Pharmacopœia directs its tincture to be made by dissolving 50 Gms. of extract of Indian hemp in sufficient alcohol to produce 1000 milliliters of tincture, and as good Indian hemp yields about 12.5 per cent. of extract, the British tincture is about 4 times as strong as our own. The tincture has a deep green color and a disagreeable heavy odor. It is precipitated by addition of water.

Tinctura Cantharidis (*Tincture of Cantharides*).—Simple maceration or percolation of powdered cantharides with alcohol has been shown not to extract the active principles fully, and digestion with alcohol for twenty-four hours with frequent agitation, at a temperature of from 50° to 55° C. (122° to 131° F.) is now directed; after this the mixture is transferred to a cylindrical percolator, allowed to drain and then percolated with sufficient alcohol to produce the required volume of tincture.

The Pharmacopœia does not direct that tincture of cantharides shall be assayed, but since it requires that cantharides shall contain not less than 0.6 per cent. of cantharidin, the tincture should, if exhaustion of the drug has been fairly complete, contain about 0.0006 Gm. of cantharidin in each mil. (or Cc.).

Tinctura Cinchonæ (*Tincture of Cinchona*).—This preparation should be made from assayed cinchona bark yielding not less than 6 per cent. of total alkaloids. It is twice as rich in alkaloids as the compound tincture of cinchona, and is made from yellow cinchona bark, also known as calisaya bark. The Pharmacopœia requires that 100 mils. (or Cc.) of tincture of cinchona, when assayed, shall yield not less than 0.9 Gm. nor more than 1.1 Gms. of the total alkaloids of the drug.

Tinctura Cinchonæ Composita (*Compound Tincture of Cinchona*).—The Pharmacopœia directs red cinchona bark to be used in making this tincture, and requires that 100 mils. (or Cc.) of the finished product, when assayed, shall yield not less than 0.45 Gm. nor more than 0.55 Gm. of the total alkaloids of cinchona. The presence of bitter orange peel and serpentaria does not interfere with the assay of the tincture, as neither drug contains any alkaloid. The tincture has a brownish-red color and a very bitter taste. In this as well as in the preceding tincture the use of a strongly alcoholic menstruum with the addition of glycerin prevents the deposit of cinchona red, an oxidation product of cincho-tannic acid.

Tinctura Colchici Seminis (*Tincture of Colchicum Seed*).—The activity of colchicum resides in the alkaloid colchicine, and the tincture should

always be made from assayed seed containing not less than 0.45 per cent. of this alkaloid. The Pharmacopœia requires that 100 mils. (or Cc.) of the tincture, when assayed, shall yield not less than 0.036 Gm. nor more than 0.44 Gm. of colchicine.

Tinctura Digitalis (*Tincture of Digitalis*).—The menstruum heretofore used for galenical preparations of digitalis, diluted alcohol, has been found not to preserve the therapeutic value of these preparations for any considerable time, and hence a menstruum 50 per cent. stronger in alcohol is now directed, which experience has shown to be satisfactory.

While the Pharmacopœia does not demand that tincture of digitalis shall be standardized, it states that if assayed biologically, the minimum lethal dose should not be greater than 0.006 mil. (or Cc.), or the equivalent in tincture of 0.0000005 Gm. of ouabain, for each gram of body weight of the frog used in the experiment.

Tinctura Ferri Chloridi (*Tincture of Ferric Chloride*).—When an aqueous solution of ferric chloride is mixed with alcohol, as in the official process, contraction of volume occurs, and a subsequent addition of alcohol is necessary to bring the finished product up to the required volume; furthermore, a rather pleasant ethereal odor is gradually developed, due to chemical reaction between the acid and alcohol. The pharmacopœial directions to allow the mixture to stand for three months at least before dispensing it, are intended to insure uniformity by bringing all changes to completion, but it is questionable whether the time stated is sufficient for this purpose. When tincture of ferric chloride is exposed to light, the iron salt is slowly reduced to the ferrous state, the color of the tincture gradually changing to olive-brown, and hence it should be kept in amber-colored bottles.

Since the official solution of ferric chloride contains about 30 per cent. of anhydrous salt, the specific gravity of the solution being given as 1.30 at 25° C (77° F.), the 350 mils. (or Cc.) directed for the preparation of 1000 mils. (or Cc.) of the tincture will contain about 136.5 Gms., and as the specific gravity of the tincture is given as 1.000 at 25° C. (77° F.), each mil. (or Cc.) will contain about 0.1365 Gm. of the anhydrous salt.

Tinctura Gambir Composita (*Compound Tincture of Gambir*, also known as *Tincture of Pale Catechu*).—The official tincture has a reddish-brown color and a strongly astringent taste. It may be dispensed when tincture of catechu or compound tincture of catechu is prescribed. True catechu not being available in the market any longer, gambir, also known as pale catechu, is now used in its stead.

Tinctura Gentianæ Composita (*Compound Tincture of Gentian*).—The increased alcoholic strength of the menstruum directed in the last Pharmacopœia having failed to prevent precipitation, it has been reduced in the present official formula and glycerin has been added with the view of overcoming the difficulty.

Tinctura Hydrastis (*Tincture of Hydrastis*).—Although hydrastis contains other alkaloids besides hydrastine, the latter is considered

as the most important medicinally; it is soluble in ether while berberine is not. The Pharmacopœia requires that 100 mils. (or Cc.) of the tincture, when assayed, shall yield not less than 0.36 Gm. nor more than 0.44 Gm. of the ether-soluble alkaloids of the drug. It is not miscible with aqueous liquids without precipitation, on account of the resinous matter present.

Tinctura Hyoscyami (*Tincture of Hyoscyamus*).—The present official tincture is weaker than formerly. Hyoscyamus is very variable in its alkaloidal content and some of the commercial article is of poor quality, hence the assayed drug alone should be used for making the tincture. The Pharmacopœia requires that 100 mils. (or Cc.) of tincture of hyoscyamus, when assayed, shall yield not less than 0.0055 Gm. nor more than 0.0075 Gm. of the total alkaloids of the drug.

Tinctura Iodi (*Tincture of Iodine*).—The solution of the iodine in a concentrated aqueous solution of potassium iodide materially facilitates the preparation of the tincture. The addition of potassium iodide serves a double purpose; it is made mainly to prevent or at least to retard, the formation of hydriodic acid and thus maintains the iodine strength of the tincture, and it also prevents precipitation when the tincture is mixed with water.

The Pharmacopœia requires that 100 mils. (or Cc.) of tincture of iodine, when assayed, shall contain not less than 6.5 Gms. nor more than 7.5 Gms. of iodine and not less than 4.5 Gms. nor more than 5.5 Gms. of potassium iodide.

Tinctura Kino (*Tincture of Kino*).—In order to better protect this tincture against gelatinization it should be preserved in a cool place, in well-stoppered small vials of 1- or 2-oz. capacity, thus obviating frequent exposure to air.

Tinctura Lactucarii (*Tincture of Lactucarium*).—The object of treating the lactucarium with purified petroleum benzin is to remove lactucerin and caoutchouc-like matters, the active principles, lactucin, latucic acid, and lactucopicrin, not being affected by that liquid. In order finally to get rid of all benzin odor, the residue should be dried in a current of warm air. The subsequent percolation of the powder mixed with sand presents no difficulty, the active principles being all soluble in diluted alcohol, but in order to insure complete exhaustion, the percolate should be collected very slowly. If carefully made the tincture is miscible with glycerin and syrup without precipitation.

Tinctura Limonis Corticis (*Tincture of Lemon Peel*).—This tincture is of the same strength as the tincture of sweet orange peel and made in the same manner. It is intended to replace the spirit of lemon of former pharmacopœias, and is of much finer flavor than the latter.

Tinctura Moschi (*Tincture of Musk*).—The preliminary maceration of the musk with water for twenty-four hours is intended to facilitate the extraction of the active odorous principles, which are soluble in water. The finished tincture represents 0.05 Gm. of musk in each mil. (or Cc.), or about $3\frac{1}{5}$ grains in a fluidrachm, which latter seems

hardly sufficient for an average dose; as an antispasmodic, musk is frequently given in doses of 5 to 10 grains.

Tinctura Nucis Vomicæ (*Tincture of Nux Vomica*).—The former directions to prepare this tincture by solution of standardized extract of nux vomica in a hydroalcoholic menstruum have been dropped and percolation of the crude drug with a strongly alcoholic menstruum is now directed. Nux vomica containing between 2.5 and 3 per cent. of total alkaloids should be used, and percolation be conducted at the rate of not more than 10 drops per minute. The Pharmacopœia requires that 100 mils. (or Cc.) of tincture of nux vomica, when assayed, shall yield not less than 0.237 Gm. nor more than 0.263 Gm. of the total alkaloids of the drug. The official tincture has a yellowish color and a very bitter taste, and becomes opalescent when mixed with water.

Tinctura Opii (*Tincture of Opium*).—Opium readily yields its active constituents to water, and the preliminary treatment of the coarse powder with hot water is intended to facilitate complete exhaustion by the hydroalcoholic menstruum used subsequently. The present tincture is slightly weaker than that formerly official, and contains 10 milligrams of anhydrous morphine in each mil. (or Cc.). This change was made to bring our official tincture of opium into conformity with the strength prescribed by the International Protocol adopted by all the nations party to the International Conference at Brussels in 1902. The Pharmacopœia requires that 100 mils. (or Cc.) of tincture of opium, when assayed, shall yield not less than 0.95 Gm. nor more than 1.1 Gm. of anhydrous morphine. The tincture has a deep reddish-brown color and the characteristic narcotic odor and bitter taste of opium. The name *laudanum* is officially applied to tincture of opium by the Pharmacopœia, and as such it was at one time frequently sold indiscriminately to persons addicted to the use of opium, but fortunately this very censurable practice has come under the control of the National Government by enactment of the Harrison Narcotic Law by Congress in 1914.

Tinctura Opii Deodorati (*Tincture of Deodorized Opium*).—In order to deprive opium of its peculiar nauseating principle, to which the characteristic odor of the drug is due, the Pharmacopœia directs that a concentrated infusion of opium shall be treated with two successive portions of purified petroleum benzin. This plan is preferable to the more annoying treatment with ether formerly used, because no emulsion is formed and the benzin can be easily separated from the aqueous fluid. Other methods for deodorizing infusions of opium have been suggested at different times, and the following, less troublesome than the benzin treatment and equally efficacious, has been found very satisfactory by the author and many others. It was first suggested by F. T. Gordon in 1900. An infusion obtained by exhausting 100 Gms. of granulated opium with water is concentrated to 500 mils. (or Cc.) and heated to about 82° C. (179.6° F.); 150 Gms. of paraffin, melting

at about 50° C. (122° F.), are now added in small pieces, and when liquefied the mixture is thoroughly stirred or shaken for ten minutes until the paraffin no longer seems to darken in color. After cooling the hardened crust of paraffin is broken, the deodorized liquid poured off, and the dish and under side of the paraffin washed with a little cold water, the washings being added to the decanted liquid. The mixture is filtered through paper and the filtrate made up to a volume of 750 mils. (or Cc.) by washing the filter with small quantities of water, after which 200 mils. (or Cc.) of alcohol are added; the liquid is then assayed and adjusted so that each mil. (or Cc.) shall contain 10 milligrams of anhydrous morphine. The Pharmacopœia makes the same requirement for this tincture as for tincture of opium, when assayed.

Neither the treatment with purified petroleum benzin, nor that with paraffin, removes any narcotine from the concentrated infusion of opium, which is soluble, however, in ether, and which by many is considered an important constituent of the drug.

Tincture of deodorized opium is of lighter color than the ordinary tincture of opium and without the disagreeable narcotic odor of the latter, but is directed to be of the same morphine strength.

Tinctura Physostigmatis (*Tincture of Physostigma*, also known as *Tincture of Calabar Bean*).—On account of the fatty and resinous matter present in calabar bean, strong alcohol is a better menstruum for preparing the tincture than a hydro-alcoholic mixture. The Pharmacopœia requires that 100 mils. (or Cc.), when assayed shall yield not less than 0.013 Gm. nor more than 0.017 Gm. of physostigma alkaloids; ether alone being used as a solvent for the liberated alkaloids, only the ether-soluble alkaloids will be determined, consisting chiefly of physostigmine, calabarine being insoluble in ether.

Tincture of physostigma is of a pale brownish-yellow color, and should be preserved in small, well stoppered bottles, protected from light, on account of the sensitiveness of the alkaloidal salts, when in solution, to the influence of air and light.

Tinctura Quassiæ (*Tincture of Quassia*).—While water alone will extract all the medicinal virtues of quassia, a hydro-alcoholic menstrum is prescribed and is necessary for the stability of the tincture, which has a light brownish-yellow color and a persistently bitter taste. It differs from most bitter tinctures in not being colored black or green by addition of ferric salts, since it contains no tannin.

Tinctura Sanguinariæ (*Tincture of Sanguinaria*, also known as *Tincture of Bloodroot*).—The addition of hydrochloric acid (1 per cent. by volume of the intended finished product) to the menstruum not only facilitates the extraction of the alkaloidal constituents of the drug, but also materially improves the stability of the tincture.

Tinctura Scillæ (*Tincture of Squill*).—A strongly alcoholic menstruum is directed for the purpose of avoiding solution of much mucilaginous and saccharine matter, and maceration for forty-eight hours before percolation is begun facilitates extraction of the active principles.

While the Pharmacopœia does not direct standardization for tincture of squill, it states that, if assayed biologically, the minimum lethal dose should not be greater than 0.006 mil. (or Cc.), or the equivalent in tincture of 0.0000005 Gm. of ouabain for each gram of body weight of the frog used in the experiment.

Tinctura Stramonii (*Tincture of Stramonium*).—Since stramonium leaves vary somewhat in their alkaloidal content, the tincture should be made from leaves which have been assayed, in order to insure the full amount of alkaloids in the finished product, which is 0.00025 Gm. in each mil. (or Cc.). Tincture of stramonium has a greenish-brown color and a peculiar odor reminding somewhat of belladonna leaves, but more pronounced.

The Pharmacopœia requires that 100 mils. (or Cc.) of tincture of stramonium, when assayed, shall yield not less than 0.0225 Gm. nor more than 0.0275 Gm. of the total alkaloids of the drug.

Tinctura Strophanthi (*Tincture of Strophanthus*).—In order to free the powdered seed from all fatty matter, percolation with purified petroleum benzin is directed, which makes possible a permanently clear tincture by subsequent percolation with alcohol; the benzin in no wise affects the active constituents of the drug.

While the Pharmacopœia does not require standardization of tincture of strophanthus, it states that if assayed biologically, the minimum lethal dose of the tincture should not be greater than 0.0006 mils. (or Cc.) or the equivalent in tincture of 0.0000005 Gm. of ouabain for each gram of body weight of the frog used in the experiment.

Tinctura Zingiberis (*Tincture of Ginger*).—The official tincture is directed to be made from Jamaica ginger. It is often called for as *Essence of Ginger*. The Pharmacopœia requires that if 10 Gms. of the tincture be evaporated to dryness in a tared dish on a waterbath, not more than 2 per cent. (0.2 Gm.) of residue should remain, and if this residue be treated with 20 mils. (or Cc.) of cold distilled water, not more than 15 per cent. of it should dissolve. A qualitative test is also given for the possible presence of capsicum or similar pungent substitute, depending upon the taste of the residue obtained by boiling the dry residue from 10 mils. (or Cc.) of tincture of ginger with 5 mils. (or Cc.) of half-normal alcoholic potassium hydroxide solution for thirty minutes, evaporating the alcohol, agitating with 50 mils. (or Cc.) of distilled water, filtering, shaking the filtrate out with 25 mils. (or Cc.) of ether, and evaporating the ether spontaneously, a few drops at a time, from the center of a watch glass; the taste should be camphoraceous, but not bitingly pungent.

Tinctura Vanillæ (*Tincture of Vanilla*).—This tincture has been dropped from the Pharmacopœia, but a formula for its preparation is given in the *National Formulary;* the strength of the tincture is the same as formerly and the directions for making it are similar to those of the last Pharmacopœia. It is frequently called *Extract of Vanilla*, although many of the commercial extracts of vanilla do not

correspond to this preparation, a large number being colored solutions of vanillin or vanillin and coumarin in alcohol and water, or mixtures of such solutions with tincture of vanilla, which can be readily distinguished from the tincture made from the bean by the following method: Evaporate some of the extract of vanilla on a waterbath so as to get rid of the alcohol, make up the original volume by addition of water, and acidify with acetic acid; a reddish-brown precipitate of resin will form in the case of an extract made from the bean, while absence of such resin will indicate that it was a solution of vanillin or perhaps of vanillin and coumarin. The filtrate from such resin, in the case of the official tincture, should give a copious precipitate upon the addition of solution of basic lead acetate. In case the extract was made partly from vanilla bean and partly from synthetic vanillin, the amount of precipitate must be compared with that obtained from a like quantity of extract known to be made from bean only.

It should be borne in mind that, since tincture of vanilla is used altogether as a flavoring agent, the flavor will be much improved by age, and it is a good plan to set the finished product aside for six months or longer before using.

Tincturæ Æthereæ (*Ethereal Tinctures*).—The *National Formulary* directs that when not otherwise stated, ethereal tinctures shall be made by percolating 100 Gms. of the drug, properly comminuted, with sufficient of a mixture of alcohol 1 volume and ether 3 volumes to produce 1000 mils. (or Cc.) of percolate.

Tincturæ Medicamentorum Recentium (*Tinctures of Fresh Drugs*).—According to the *National Formulary* these tinctures should be made by macerating 500 Gms. of the fresh drug, cut, bruised or crushed, with 1000 mils. (or Cc.) of alcohol for fourteen days, then strongly expressed and the liquid filtered.

These tinctures can, of course, only be made from such plants as grow in this country, and must vary in quality according to the amount of moisture present in the drug; the use of alcohol as a menstruum prevents the solution of much inert matter, and insures the presence in the finished product of all constituents soluble in a strongly alcoholic fluid.

CHAPTER XXI.

WINES AND VINEGARS.

THESE two classes of preparations are but little used by physicians, in this country, at the present time, and their number has been gradually diminished. The present Pharmacopœia has dropped all wines and recognizes but 1 vinegar.

WINES.

The Pharmacopœia no longer recognizes wines as official preparations but those formerly official have been transferred to the *National Formulary*, since some of them will no doubt be prescribed occasionally by physicians.

The *National Formulary* directs only sherry wine as a mentruum in the preparation of medicated wines, which in a number of cases is fortified by the addition of from 5 to 15 per cent. of alcohol, in order to insure stability of the solutions, especially during hot weather. While red wine as a rule contains considerable quantities of tannin, sherry wine is comparatively free from it, but if a test with ferric chloride solution shows appreciable darkening of color, the wine should be treated as directed below.

The process of freeing wines from tannin is termed detannating them, and is a very simple operation. The simplest plan is to add ½ ounce of gelatin in No. 40 or No. 60 powder to 1 gallon of the wine, and agitate occasionally during twenty-four to forty-eight hours; then filter. The operation is preferably carried out during cold weather or in a cold apartment, as heat will cause the gelatin to dissolve, and the maceration must be continued until a small portion of the wine mixed with a few drops of ferric chloride solution shows no darkening of color. Gelatin in large pieces is not suitable, especially with wines containing much tannin, since the newly formed tannate of gelatin will be deposited on the surface and prevent further intimate contact of the gelatin with the wine. As the removal of tannin from wine in no way interferes with its quality—alcoholic strength and aroma remaining the same, and only coloring matter being lost—a supply of detannated wine should be kept on hand, for it requires very little more labor to detannate a gallon than a pint.

The alcohol content of wine varies from 10 per cent. to 15 per cent., and sometimes 20 per cent., and may be determined by the method

given in the last Pharmacopœia, as follows: Take the specific gravity of the wine at 15.6° C. (60° F.), evaporate a carefully measured portion of it, in a tared capsule, to one-third of its weight, cool and restore the original volume by the addition of water, and again take the specific gravity of the liquid at 15.6° C. (60° F.); the difference between the two specific gravities subtracted from 1.000 indicates the specific gravity of an alcohol containing the same percentage of absolute alcohol as the wine, the corresponding percentage being ascertained by reference to the alcoholometric tables published in the Pharmacopœia. Suppose the wine before evaporation has a specific gravity of 0.9930, and after evaporation and addition of water, 1.0098: then 1.0098 — 0.9930 = 0.0168, and 1.000 — 0.0168 = 0.9832; by referring to the tables it is found that alcohol of 0.9832 specific gravity at 15.6° C. (60° F.) contains between 10 and 11 per cent. by weight, or between 12 and 13 per cent. by volume, of absolute alcohol.

THE MEDICATED WINES OF THE NATIONAL FORMULARY.—Of the 15 medicated wines recognized, 4 are made by percolation, and 11 by solution of the medicinal agent in the menstruum. Three of the wines are directed to be standardized to a definite alkaloidal content.

Made by Percolation.

Latin name.	English name.	Method of preparation.
Vinum Aurantii Compositum (Elixir Aurantii Compositum)	Compound Wine of Orange (Compound Elixir of Orange) . .	Made by percolating a mixture of bitter orange peel, absinthium, menyanthes leaves, cascarilla, cinnamon, and gentian, all in No. 40 powder, and potassium carbonate with sherry wine.
Vinum Colchici Cormi	Wine of Colchicum Corm (Wine of Colchicum Root) . . .	Made by percolating colchicum corm, in No. 30 powder, with a mixture of alcohol, 15 volumes, and sherry wine, 85 volumes. The wine is assayed and required to contain not less than 0.126 Gm. nor more than 0.154 Gm. of colchicine in 100 mils. (or Cc.).
Vinum Fraxini Americanæ.	Wine of White Ash . . .	Made by macerating white ash bark in No. 40 powder with sherry wine, fortified with alcohol, for 3 days, and then percolating, using sufficient menstruum to make up the required volume.
Vinum Pruni Virginianæ	Wine of Wild Cherry . .	Made by macerating wild cherry in No. 40 powder with a small quantity of water for 4 hours, then packing in a percolator, saturating with a mixture of sherry wine and alcohol, and again macerating for 12 hours. Percolation is then allowed to go on until a prescribed quantity of percolate has been collected, in which sugar is dissolved. The mixture is finally filtered with the aid of purified talc.

Made by Simple Solution.

Latin name.	English name.	Method of preparation.
Vinum Antimonii	Wine of Antimony	Made by adding a hot aqueous solution of antimony and potassium tartrate to sherry wine. Each Cc. contains 0.004 Gm. of antimony and potassium tartrate.
Vinum Carnis . .	Wine of Beef .	Made by dissolving extract of beef in hot water, adding syrup and then compound spirit of orange and alcohol, previously mixed, and finally sufficient sherry wine to make up the required volume. After 2 days, the mixture is filtered.
Vinum Carnis et Ferri	Wine of Beef and Iron (Beef, Wine, and Iron)	Made like the preceding preparation, except that after addition of the syrup, compound spirit of orange and alcohol, a solution of iron and ammonium citrate in sherry wine is added and when the required volume has been made up, the liquid, if acid, is neutralized with ammonia water, added drop by drop. After 2 days, the mixture is filtered.
Vinum Colchici Seminis	Wine of Colchicum Seed . .	Made by mixing fluidextract of colchicum seed, alcohol and sherry wine, and after 2 days filtering the mixture. The wine is required to contain not less than 0.036 Gm. nor more than 0.044 Gm. of colchicine in 100 mils. (or Cc.).
Vinum Ferri . . .	Wine of Iron (Wine of Citrate of Iron) .	Made by dissolving iron and ammonium citrate in sherry wine, adding to this solution syrup and tincture of sweet orange peel, and finally sufficient sherry wine to make up the required volume. It should be filtered after 2 days' rest.
Vinum Ferri Amarum	Bitter Wine of Iron . . .	Made by dissolving iron and quinine citrate in sherry wine, adding to this solution syrup and tincture of sweet orange peel, and finally sufficient sherry wine to make up the required volume. It should be filtered after 2 days.
Vinum Ipecacuanhæ	Wine of Ipecac .	Made by mixing fluidextract of ipecac, sherry wine and alcohol, and after 2 days filtering the mixture. The wine is required to contain not less than 0.180 Gm. nor more than 0.220 Gm. of the alkaloids of ipecac in 100 mils. (or Cc.).
Vinum Pepsini . .	Wine of Pepsin .	Made by adding glycerite of pepsin to a mixture of sherry wine and alcohol. As pepsin is apt to lose its activity if in contact with alcoholic fluids for some time, it is best to make this wine extemporaneously.

Latin name.	English name.	Method of preparation.
Vinum Picis . . .	Wine of Tar .	Made by macerating well washed tar with fortified sherry wine and pumice for 4 hours, then filtering and passing enough sherry wine through the filter to make up the required volume.
Vinum Pruni Virginianæ Ferratum .	Ferrated Wine of Wild Cherry .	Made by adding tincture of citrochloride of iron to wine of wild cherry.
Vinum Rhei Compositum	Compound Wine of Rhubarb .	Made by mixing fluidextract of rhubarb, fluidextract of bitter orange peel, tincture of cardamom and sugar with sherry wine, and agitating until solution is effected.

VINEGARS.

The valuable solvent as well as preservative properties of diluted acetic acid were at one time employed for a larger class of preparations than at present, of which the vinegar of squill alone is now recognized in the Pharmacopœia. The official diluted acetic acid is made by mixing 1 part of 36 per cent. acetic acid with 5 parts of water, and contains, therefore, 6 per cent. of absolute acetic acid.

VINEGARS RECOGNIZED IN THE PHARMACOPŒIA AND NATIONAL FORMULARY.

Latin name.	English name.	Method of preparation.
Acetum Aromaticum Nat. Form.	Aromatic Vinegar	A solution of the oils of lavender, rosemary, juniper, peppermint, cinnamon, lemon and cloves in alcohol, with the addition of acetic acid and water. The mixture is set aside for 8 days and filtered.
Acetum Opii . . . Nat. Form.	Vinegar of Opium	Made by macerating granulated opium, powdered nutmeg and sugar with diluted acetic acid for 7 days and then percolating the mixture, enough diluted acetic acid being finally poured on the dregs to make up the required volume of percolate.
Acetum Scillæ . . U. S. P.	Vinegar of Squill	Made by macerating squill, in coarse powder, with diluted acetic acid for 7 days, with frequent stirring, after which the mixture is strained and the dregs washed with sufficient acetic acid to make up the required volume.

CHAPTER XXII.

FLUIDEXTRACTS.

THE term fluidextract, in its present acceptation, is applied to concentrated alcoholic or hydroalcoholic solutions of vegetable principles, which are permanent and represent all the active virtues of the drugs from which they are made; they are officially recognized in the pharmacopœias of the United States, Great Britain, Germany, France, and Switzerland, differing but slightly in strength in the five countries.

Fluidextracts, or liquid extracts, as they are called in Great Britain, were first introduced about 1832. Prior to 1847 little interest appears to have been taken in this class of preparations in the United States, only 3 fluidextracts being on record as in use at that time—namely, those of senna, valerian, and rhubarb; from that time forward fluidextracts grew in favor, and the Pharmacopœia of 1850 gave working formulas for 7 concentrated solutions, of which, however, only 1 (valerian) is deserving of the title of fluidextract in the present definition of that term; 2 were oleoresins (cubebs and black pepper), and 4 concentrated syrups (rhubarb, sarsaparilla, senna, and spigelia and senna). In 1860 the number of fluidextracts officially recognized was increased to 25, in 1870 to 46, in 1880 to 79, in 1890 to 88, in 1900 reduced to 85, and in the present (ninth) revision of the Pharmacopœia still further reduced to 49. Besides these a large number of unofficial fluidextracts are annually produced, and this class of preparations must be considered as the most important galenicals used by physicians.

Prior to 1880 the strength of fluidextracts, as prescribed by the Pharmacopœia, was 1 grain of drug to 1 minim of fluidextract; since that time the pharmacopœial strength is based upon the relation of the metric measures of weight and capacity, so that any weight of a given drug is to be converted into a fluidextract having the bulk of the same weight of water at its maximum density, or, in other words, 1 Gm. of the drug is represented by 1 mil. (or Cc.) of the fluidextract. The exceptions to this rule are the fluidextracts of aconite, belladonna root, cinchona, colchicum seed, hydrastis, hyoscyamus, guarana, ipecac, nux vomica, pilocarpus, and stramonium, all of which are directed to be standardized to definite alkaloidal strength. British liquid extracts, with the exception of those of belladonna, cinchona, hydrastic, ipecac, licorice, nux vomica, and opium, are made of the same strength as our own fluidextracts; the alkaloidal liquid extracts are also standardized to a definite alkaloid content. In France,

Germany, and Switzerland each Gm. of drug is represented by 1 Gm. of fluidextract, the relation being weight for weight.

All the official fluidextracts are directed to be prepared by percolation, a menstruum uniform in alcoholic strength being employed during the process of exhaustion. When, however, glycerin is used with the first portion of the menstruum, percolation is continued and finished with a liquid of the same alcoholic strength, but not mixed with glycerin. By evaporating the weak percolate to a soft extract, most of the water is also expelled, and the comparatively small portion remaining with the extract will occasion but a slight change in the menstruum of the reserved portion, which, at the same time, is the best solvent for the extractive matter; finally, the addition of fresh menstruum will not change the alcoholic strength of the liquid.

The official directions for the preparation of fluidextracts are intended for the quantity of drug designated in the formulas, and must of necessity often be modified by manufacturers who operate upon hundreds of pounds at one time; fineness of powder, degree of packing, and rate of percolation must be adapted to the quantity of material in hand. Manufacturers in some cases resort to repeated maceration and expression instead of percolation.

All fluidextracts, no matter how carefully made, will begin to deposit soon after they are completed, and this precipitation will continue for a varying length of time. The menstruum dissolves certain extractive principles which it is incapable of retaining in perfect solution afterward under changes of temperature, and thus far no method is known to prevent entirely such separation, which is augmented by exposure to light, air, and heat. Fluidextracts prepared without heat are less prone to deposit than when made by the official process, and in these the amount of precipitate is often very trifling; happily, frequent examinations of precipitates in fluidextracts have disclosed the facts that they consist chiefly of inert extractive matter, and therefore do not affect the medicinal value of the preparation. All freshly made fluidextracts should be set aside in well stoppered glass vessels, in dark and moderately cool places, for a period of two or three months, before filtering and bottling them; this plan is universally followed by large manufacturers, and explains the absence, in many cases, of appreciable deposits. Decantation is preferable to filtering in large operations, as there is less loss of alcohol; the liquid is allowed to precipitate in a cylindrical vessel with a stopcock arranged a little above the bottom of the vessel.

In the case of those fluidextracts which are to be standardized to contain a definite quantity of alkaloid in every milliliter, the Pharmacopœia does not direct the finished product to be brought up to the volume of 1000 mils. After dissolving the soft extract, obtained by evaporation of the weak percolate, in the reserve portion, the whole is thoroughly mixed and a portion of the liquid then assayed; from the results thus obtained, the amount of alkaloids in the remainder of the

liquid is calculated, and sufficient menstruum is added to bring the fluidextract up to the required standard. This modification applies to fluidextracts made by either Process A or Process B. In the case of fluidextracts made by Process C a different modification is ordered, only 420 mils. (or Cc.) of percolate being collected from the third portion of drugs instead of the 500 mils. (or Cc.) directed in the process; this percolate is mixed with the two portions of percolate previously reserved, a sample of the mixture is then assayed and the alkaloidal content of the remainder of the liquid having been calculated, the proper volume is adjusted by addition of menstruum.

The quantity of alcohol in finished fluidextracts is not the same as the amount of alcohol in the menstrua employed, which fact is due to loss by evaporation during manufacture, variations in the amount of water in the air-dried drugs and the absorption of moisture from the air; hence if the percentage of alcohol in the finished product is wanted, it must be determined by distillation, as directed in the U. S. P.

The Pharmacopœia classifies the official fluidextracts according to the menstruum employed for extraction of the drug and the particular process of manufacture used, thus:

CLASS A. This includes those fluidextracts made by the usual process of percolation with an alcoholic or hydroalcoholic menstruum, namely, the fluidextracts of belladonna root, buchu, cannabis, cimicifuga, colchicum seed, digitalis, eriodictyon, eucalyptus, gelsemium, gentian, grindelia, guarana, hyoscyamus, nux vomica, pilocarpus podophyllum, rhubarb, sabal, sarsaparilla, senna, spigelia, stavisagria, stillingia, sumbul, veratrum viride, viburnum prunifolium, xanthoxylum, and zingiber.

The official process of manufacture for this class directs that the powdered drug be moistened with sufficient of the prescribed menstruum to dampen it uniformly and to so maintain it after six hours' maceration in a tightly covered vessel. The damp drug is then packed in a cylindrical percolator (more or less firmly according to the nature of the drug) and enough menstruum is poured on to thoroughly saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, the lower orifice is closed, the percolator closely covered and the drug allowed to macerate for forty-eight hours. Percolation is then allowed to proceed slowly, at a rate not to exceed 10 drops per minute, until 850 mils. (or Cc.) of percolate have been collected for every 1000 Gms. of drug used, fresh menstruum being gradually added in order to maintain a constant layer of liquid above the column of drug in the percolator. This first percolate is set aside as reserve tincture and percolation then continued at a rate not to exceed 20 drops per minute until the drug is exhausted, fresh menstruum being supplied as before. The alcohol is recovered from the weak percolate, which is then evaporated to the consistence of a soft extract at a temperature not exceeding 60° C. and dissolved in the reserve tincture. Finally sufficient menstruum

is added to bring the volume up to 1000 mils. (or Cc.) for every 1000 Gms. of drug used, or the proper volume required as shown by the assay standard. The whole is thoroughly mixed by agitation.

CLASS B. This includes those fluidextracts in which glycerin or an acid is used in extracting the drug, two menstrua being successively used. Menstruum I contains the glycerin or acid in definite proportion to the amount of drug; Menstruum II consists of a mixture of alcohol and water to be used for completing the extraction of the drug. To this class belong the fluidextracts of cinchona, ergot, hydrastis, ipecac, lobelia, pomegranate, quebracho, rose, compound sarsaparilla, taraxacum, and uva ursi.

The official process of manufacture for this class directs that the powdered drug be moistened with sufficient of the prescribed Menstruum I to dampen it uniformly and to so maintain it after six hours' maceration in a tightly covered vessel. The damp drug is then packed in a cylindrical percolator, the remainder of Menstruum I is poured on and, when this has just disappeared from the surface, Menstruum II is gradually added, a layer of liquid being constantly maintained above the drug. When the liquid begins to drop from the percolator, the lower orifice is closed, the percolator closely covered and the drug allowed to macerate for forty-eight hours. Percolation is then allowed to proceed slowly at a rate not to exceed 10 drops per minute, Menstruum II being added as required, until 850 mils. (or Cc.) of percolate have been collected for every 1000 Gms. used. This is set aside as reserve tincture and percolation continued at a rate not to exceed 20 drops per minute, until the drug is exhausted, Menstruum II being supplied as before. The alcohol is recovered from the weak percolate, which is then evaporated to the consistence of a soft extract at a temperature not exceeding 60° C. and dissolved in the reserve tincture. Finally sufficient Menstruum II is added to bring the volume up to 1000 mils. (or Cc.) for every 1000 Gms. of drug employed, or the proper volume required as shown by the assay standard. The whole is thoroughly mixed by agitation.

CLASS C. This class includes more especially the fluidextracts of drugs containing volatile ingredients or constituents likely to be injured by exposure to heat, thus: the fluidextracts of aconite, aromatic powder and bitter orange peel.

The official process of manufacture for this class of fluidextracts is designated as that of fractional or divided percolation, and may be used as an alternative process for the fluidextracts mentioned in Class A. 1000 Gms. of the drug are divided into three parts of 500 Gms., 300 Gms. and 200 Gms., respectively. The first portion (500 Gms.) is moistened with sufficient of the prescribed menstruum to dampen the drug uniformly and so maintain it after six hours' maceration in a tightly covered vessel. It is then packed in a cylindrical percolator, sufficient menstruum being poured on to saturate the powder and leave a stratum of liquid above it. When the liquid begins to drop

from the percolator, the lower orifice is closed, the percolator closely covered, and the drug allowed to macerate for forty-eight hours. Percolation is then allowed to go on at a rate not to exceed 10 drops per minute, menstruum being gradually poured on to maintain a constant layer above the drug. The first 200 mils. (or Cc.) of percolate are set aside as a reserve and percolation continued until 1500 mils. (or Cc.) of additional percolate have been collected in successive portions of 300 mils. (or Cc.) each. (To avoid confusion the weaker percolates should be numbered 1, 2, 3, 4, and 5.)

The second portion of the drug (300 Gms.) is moistened with sufficient of the first weaker percolate to render it uniformly damp and so maintain it after six hours' maceration in a tightly covered vessel. It is then packed in a cylindrical percolator, macerated, and percolated as in the case of the first portion of the drug, but using as menstruum the weak percolates in the order in which they were collected, followed, if these be insufficient, by some of the original menstruum. The first 300 mils. (or Cc.) of percolate are set aside as reserve and percolation continued until 600 mils. (or Cc.) of weaker percolate have been collected in successive portions of 200 mils. (or Cc.) each.

The third portion of the drug (200 Gms.) is moistened with sufficient of the first portion of weaker percolate collected from the second portion of the drug to render it uniformly damp and so maintain it after six hours' maceration in a tightly covered vessel. It is then packed in a cylindrical percolator, and macerated and percolated as in the case of the second portion of the drug, using as menstruum the remaining portions of weaker percolate from the preceding operation in the order in which they were collected, followed, if necessary, by some of the original menstruum. Collect 500 mils. (or Cc.) of percolate and mix this with the two portions of reserve previously set aside, so as to bring the volume up to 1000 mils. (or Cc.).

In the case of fluidextracts to be adjusted by assay to a definite alkaloidal standard, collect only 420 mils. (or Cc.) of percolate from the third portion of drug instead of the 500 mils. (or Cc.) directed above. Mix this percolate with the two portions previously reserved, assay a portion of the mixture and adjust its volume by the addition of the menstruum directed, so that each 100 mils. (or Cc.) of the finished fluidextract will contain the prescribed amount of alkaloid.

This process, sometimes also designated as repercolation, has the advantage that no heat whatever is applied to any part of the percolate and is admirably adapted for some drugs, especially those which yield their medicinal constituents readily to the menstruum, but in the writer's experience has not shown entirely satisfactory results in the case of alkaloidal drugs, owing to incomplete extraction of the active principles; this latter difficulty is overcome by subsequent standardization of the liquid. To insure better exhaustion, it is advisable to maintain the rate of flow of the percolate throughout the whole operation at not more than 10 drops per minute.

CLASS D. This class includes those fluidextracts made with boiling water as a menstruum, alcohol being subsequently added to the concentrated infusion as a preservative, and comprises the fluidextracts of cascara sagrada, frangula, and triticum.

The official process directs that 1000 Gms. of the ground drug be thoroughly mixed with 5000 mils. (or Cc.) of boiling water and allowed to macerate of two hours in a covered vessel in a warm place. The mixture is then placed in a well tinned or enamelled metallic percolator, boiling water being gradually added until the drug is exhausted. The percolate is evaporated on a boiling waterbath, or a steambath, to the volume specified under each drug and when cold the prescribed quantity of alcohol is added and thoroughly mixed.

UNCLASSIFIED. Several official fluidextracts, owing to the peculiar nature of the respective drugs from which they are made, cannot be included in any one of the preceding classes and the Pharmacopœia gives special formulas for their preparation. These are the fluidextracts of glycyrrhiza, senega, squill, and aromatic fluidextract of cascara sagrada.

Concentration of the weak percolate is usually effected by distilling off the alcohol in a suitable apparatus on a waterbath, and finally evaporating the liquid, in a porcelain capsule, to the proper consistence, preferably with constant stirring. The Pharmacopœia specifies a temperature not exceeding 60° C. (140° F.) for evaporation, which should be carefully maintained, so as to avoid changes in the extractive as far as possible.

Arranged according to the menstruum, the fluidextracts of the Pharmacopœia may be divided into 15 classes, as follows:

Made with alcohol:

Fluidextract of Aromatic Powder, Fluidextract of Buchu, Fluidextract of Cannabis, Fluidextract of Cimicifuga, Fluidextract of Ginger, Fluidextract of Podophyllum, Fluidextract of Staves-acre, Fluidextract of Veratrum Viride.

Made with alcohol 5 volumes, water 1 volume:

Fluidextract of Belladonna Root, Fluidextract of Digitalis.

Made with alcohol 4 volumes, water 1 volume:

Fluidextract of Eriodictyon, Fluidextract of Gelsemium, Fluidextract of Rhubarb, Fluidextract of Sabal, Fluidextract of Sumbul.

Made with alcohol 3 volumes, water 1 volume:

Fluidextract of Aconite, Fluidextract of Bitter Orange, Fluidextract of Eucalyptus, Fluidextract of Grindelia, Fluidextract of Guarana, Fluidextract of Hyoscyamus, Fluidextract of Nux Vomica, Fluidextract of Xanthoxylum.

Made with alcohol 2 volumes, water 1 volume:

Fluidextract of Colchicum Seed, Fluidextract of Pilocarpus, Fluidextract of Squill, Fluidextract of Senega, Fluidextract of Viburnum Prunifolium.

Made with alcohol 1 volume, water 1 volume (diluted alcohol):
Fluidextract of Ergot (with hydrochloric acid), Fluidextract of Gentian, Fluidextract of Lobelia (with acetic acid), Fluidextract of Sarsaparilla, Fluidextract of Spigelia, Fluidextract of Stillingia.

Made with alcohol 2 volumes, water 3 volumes:
Fluidextract of Ipecac (with hydrochloric acid).

Made with alcohol 1 volume, water 2 volumes:
Fluidextract of Senna.

Made with alcohol 8 volumes, water 1 volume, glycerin 1 volume; followed by a mixture of alcohol 4 volumes, water 1 volume:
Fluidextract of Cinchona (with hydrochloric acid).

Made with alcohol 6.7 volumes, glycerin 1.1 volumes, water 2.2 volumes; followed by a mixture of alcohol 2 volumes, water 1 volume:
Fluidextract of Aspidosperma.

Made with alcohol 6 volumes, water 3 volumes, glycerin 1 volume; followed by a mixture of alcohol 2 volumes, water 1 volume:
Fluidextract of Hydrastis.

Made with alcohol 5 volumes, glycerin 1 volume, water 4 volumes; followed by diluted alcohol:
Fluidextract of Pomegranate, Fluidextract of Rose, Fluidextract of Sarsaparilla (Compound), Fluidextract of Taraxacum.

Made with alcohol 3 volumes, water 5 volumes, glycerin 1 volume; followed by a mixture of alcohol 1 volume, water 2 volumes:
Fluidextract of Uva Ursi.

Made with boiling water:
Fluidextract of Cascara Sagrada, Aromatic Fluidextract of Cascara Sagrada, Fluidextract of Frangula, Fluidextract of Triticum. The finished product contains 25 per cent. by volume of official alcohol as a preservative, in the case of the three first named fluidextracts, and 20 per cent. in the case of fluidextract of triticum.

Made with a mixture of chloroform water 27 volumes and ammonia water 3 volumes:
Fluidextract of Glycyrrhiza; 25 per cent. of official alcohol is finally added as a preservative.

The *National Formulary* gives directions for the preparation of 90 fluidextracts, of which 1 is to be standardized biologically, 4 to definite alkaloidal content, and the remaining 85 are to be of the same strength as the non-standardized fluidextracts of the Pharmacopœia, namely, 1 mil. (or Cc.) represents the medicinal activity of 1 Gm. of the drug. With 3 exceptions (the fluidextracts of chestnut leaves, cinchona (aqueous), and wild cherry) the fluidextracts of the *National Formulary* are prepared according to one of the type processes (A, B, C or D) directed in the Pharmacopœia, the particular process being indicated in each case.

Arranged according to the menstruum employed, the fluidextracts of the *National Formulary* may be divided into 22 classes, as follows:

Made with alcohol only:

Fluidextract of Angelica Root, Fluidextract of Boldo, Fluidextract of Calendula, Fluidextract of Celery Fruit, Fluidextract of Cottonroot Bark, Fluidextract of Cubeb, Fluidextract of Iris Versicolor, Fluidextract of Jalap, Fluidextract of Lupulin, Fluidextract of Thuja.

Made with a mixture of alcohol 9 volumes, water 1 volume:

Fluidextract of Paracoto Bark.

Made with a mixture of alcohol 4 volumes, water 1 volume:

Fluidextract of Dioscorea, Fluidextract of Echinacea, Fluidextract of Euonymus, Fluidextract of Mezereum, Fluidextract of Serpentaria, Fluidextract of Valerian.

Made with a mixture of alcohol 3 volumes, water 1 volume:

Fluidextract of Adonis, Fluidextract of Baptisia, Fluidextract of Buchu (Compound), Fluidextract of Caulophyllum, Fluidextract of Chionanthus, Fluidextract of Cocillana, Fluidextract of Convallaria Root, Fluidextract of Corydalis, Fluidextract of Damiana, Fluidextract of Fucus, Fluidextract of Matico, Fluidextract of Trillium.

Made with a mixture of alcohol 2 volumes, water 1 volume:

Fluidextract of Aralia, Fluidextract of Colchicum Corm, Fluidextract of Convallaria Flowers, Fluidextract of Drosera, Fluidextract of Kola, Fluidextract of Parsley Root, Fluidextract of Senecio, Fluidextract of Solanum, Fluidextract of Stramonium, Fluidextract of Viburnum Opulus.

Made with a mixture of alcohol 5 volumes, water 3 volumes:

Fluidextract of Hops.

Made with a mixture of alcohol 3 volumes, water 2 volumes:

Fluidextract of Hydrangea, Fluidextract of Kava.

Made with a mixture of alcohol 1 volume, water 1 volume (diluted alcohol):

Fluidextract of Aletris, Fluidextract of Arnica Flowers, Fluidextract of Asclepias, Fluidextract of Berberis, Fluidextract of Chimaphila, Fluidextract of Chirata, Fluidextract of Condurango, Fluidextract of Conium (with acetic acid), Fluidextract of Coptis, Fluidextract of Cyprepedium, Fluidextract of Dulcamara, Fluidextract of Eupatorium, Fluidextract of Euphorbia Pilulifera, Fluidextract of Galega, Fluidextract of Helianthemum, Fluidextract of Helonias, Fluidextract of Juniper, Fluidextract of Lappa, Fluidextract of Leptandra, Fluidextract of Pareira, Fluidextract of Phytolacca, Fuidextract of Rhamnus Cathartica, Fluidextract of Rubus, Fluidextract of Rumex, Fluidextract of Scoparius, Fluidextract of Scutellaria, Fluidextract of Trifolium, Fluidextract of Verbascum, Fluidextract of Verbena, Fluidextract of Zea.

Made with a mixture of alcohol 3 volumes, water 4 volumes:

Fluidextract of Catnip.

Made with a mixture of alcohol 1 volume, water 2 volumes:
Fluidextract of Quassia.

Made with a mixture of alcohol 8 volumes, glycerin 1 volume, water 1 volume; followed by a mixture of alcohol 4 volumes, water 1 volume:
Fluidextract of Calumba.

Made with a mixture of alcohol 6 volumes, glycerin 1 volume, water 3 volumes; followed by a mixture of alcohol 3 volumes, water 2 volumes:
Fluidextract of Apocynum, Fluidextract of Geranium.

Made with a mixture of alcohol 3 volumes, strong solution of citric acid (100 Gm. in 250 mils. (or Cc.)) 1 volume; followed by a mixture of alcohol 3 volumes, water 1 volume:
Fluidextract of Sanguinaria.

Made with a mixture of alcohol 5 volumes, glycerin 2.5 volumes, water 2.5 volumes; followed by diluted alcohol:
Fluidextract of Stillingia (compound).

Made with a mixture of alcohol 5 volumes, glycerin 1 volume, water 4 volumes; followed by diluted alcohol:
Fluidextract of Juglans, Fluidextract of Krameria, Fluidextract of Quercus, Fluidextract of Rhus Glabra.

Made with a mixture of alcohol 3 volumes, glycerin 1 volume, water 5 volumes; followed by a mixture of alcohol 1 volume, water 2 volumes:
Fluidextract of Hamamelis Leaves.

Made with a mixture of alcohol 2.5 volumes, glycerin 1 volume, water 6.5 volumes; followed by a mixture of alcohol 1 volume, water 3 volumes:
Fluidextract of Thyme.

Made with a mixture of alcohol 2.5 volumes, glycerin 0.65 volume, water 6.85 volumes; followed by a mixture of alcohol 1 volume, water 3 volumes:
Fluidextract of Coffee.

Made with a mixture of glycerin 1.5 volumes, diluted alcohol 8.5 volumes; followed by diluted alcohol:
Fluidextract of Cornus.

Made with a mixture of glycerin, 1 volume, water 2 volumes; followed by a mixture of alcohol 2.5 volumes, water 1.5 volumes, and then by a mixture of alcohol 1 volume, water 3 volumes:
Fluidextract of Wild Cherry.

Made with a mixture of hydrochloric acid 3 volumes, glycerin 12.5 volumes, water 50 volumes; followed by water:
Fluidextract of Cinchona (aqueous).

Made with boiling water, followed by water; the finished product contains about 20 per cent. by volume of alcohol and 10 per cent. by volume of glycerin, added as preservatives:
Fluidextract of Chestnut Leaves.

Alphabetical List of Official Fluidextracts.

Showing the fineness of powder, the menstruum, the type, process of manufacture and the quantity of reserve percolate directed by the Pharmacopœia.

Name.	Fineness of powder.	Menstruum.	Type process of manufacture	Reserve percolate.
Fluidextract of—				
Aconite	No. 40	Alcohol 3 vols.; Water 1 vol.	C.	None
Aromatic Powder	.....	Alcohol	C.	None.
Aspidosperma	No. 30	Alcohol 670 mils.; Glycerin 110 mils.; Water 220 mils.; followed by Alcohol 2 vols. Water 1 vol.	B.	850 mils.
Belladonna Root	No. 40	Alcohol 5 vols.; Water 1 vol.	A.	800 mils.
Bitter Orange Peel	No. 20	Alcohol 3 vols.; Water 1 vol.	C.	None.
Buchu	No. 40	Alcohol.	A.	850 mils.
Cannabis	No. 30	Alcohol.	A.	850 mils.
Cascara Sagrada	No. 40	Boiling Water.	D.	None.
Cascara Sagrada (Aromatic)	No. 40	Boiling Water.	D.	None.
Cimicifuga	No. 40	Alcohol.	A.	850 mils.
Cinchona	No. 40	Alcohol 800 mils.; Glycerin 100 mils.; Diluted Hydrochloric Acid 100 mils.; followed by Alcohol 4 vols.; Water 1 vol.	B.	850 mils.
Colchicum Seed	No. 40	Alcohol 2 vols.; Water 1 vol.	A.	850 mils.
Digitalis	No. 30	Alcohol 5 vols.; Water 1 vol.	A.	850 mils.
Ergot	No. 40	Diluted Alcohol 980 mils.; Hydrochloric Acid 20 mils.; followed by Diluted Alcohol.	B.	850 mils.
Eriodictyon	No. 30	Alcohol 4 vols.; Water 1 vol.	A.	800 mils.
Eucalyptus	No. 30	Alcohol 3 vols.; Water 1 vol.	A.	800 mils.
Frangula	No. 30	Boiling Water.	D.	None.
Gelsemium	No. 40	Alcohol 4 vols.; Water 1 vol.	A.	850 mils.
Gentian	No. 30	Diluted Alcohol.	A.	850 mils.
Ginger	No. 40	Alcohol.	A.	850 mils.
Glycyrrhiza	No. 30	Chloroform; Water 2700 mils.; Ammonia; Water 300 mils.	Unclassified.	500 mils.
Grindelia	No. 30	Alcohol 3 vols.; Water 1 vol.	A.	850 mils.
Guarana	No. 60	Alcohol 3 vols.; Water 1 vol.	A.	800 mils.
Hydrastis	No. 40	Alcohol 600 mils.; Glycerin 100 mils.; Water 200 mils.; followed by Alcohol 2 vols. Water 1 vol.	B.	750 mils.
Hyoscyamus	No. 40	Alcohol 3 vols.; Water 1 vol.	A.	850 mils.
Ipecac	No. 60	Alcohol 200 mils.; Diluted Hydrochloric acid 100 mils.; Water 200 mils.; followed by Alcohol 2 vols. Water 3 vols.	B.	800 mils.
Lobelia	No. 30	Alcohol 500 mils.; Acetic acid 50 mils.; Water 450 mils.; followed by Diluted Alcohol.	B.	850 mils.
Nux Vomica	No. 40	Alcohol 3 vols.; Water 1 vol.	A.	800 mils.
Pilocarpus	No. 30	Alcohol 3 vols.; Water 1 vol.	A.	800 mils.
Podophyllum	No. 40	Alcohol.	A.	850 mils.
Rhubarb	No. 30	Alcohol 4 vols.; Water 1 vol.	A.	850 mils.
Rose	No. 20	Alcohol 500 mils.; Glycerin 100 mils.; Water 400 mils.; followed by Diluted Alcohol.	B.	850 mils.
Sabal	No. 20	Alcohol 4 vols.; Water 1 vol.	A.	850 mils.
Sarsaparilla	No. 20	Diluted Alcohol.	A.	850 mils.
Sarsaparilla (Compound)	No. 30	Alcohol 500 mils.; Glycerin 100 mils.; Water 400 mils.; followed by Diluted Alcohol.	B.	850 mils.
Senega	No. 30	Alcohol 2 vols.; Water 1 vol.	Not classified.	800 mils.
Senna	No. 40	Alcohol 1 vol.; Water 2 vols.	A.	800 mils.
Spigelia	No. 40	Diluted Alcohol.	A.	850 mils.
Squill	No. 20	Alcohol 2 vols.; Water 1 vol.	Not classified.	None.
Stavesacre	No. 20	Alcohol.	A.	850 mils.
Stillingia	No. 30	Diluted Alcohol.	A.	850 mils.
Sumbul	No. 30	Alcohol 4 vols.; Water 1 vol.	A.	850 mils.
Taraxacum	No. 30	Alcohol 500 mils.; Glycerin 100 mils.; Water 400 mils.; followed by Diluted Alcohol.	B.	850 mils.
Triticum	Finely cut.	Boiling Water.	D.	None.
Uva Ursi	No. 30	Alcohol 300 mils.; Glycerin 100 mils.; Water 500 mils.; followed by Alcohol 1 vol.; Water 2 vols.	B.	800 mils.
Veratrum Viride	No. 40	Alcohol.	A.	850 mils.
Viburnum Prunifolium	No. 30	Alcohol 2 vols.; Water 1 vol.	A.	850 mils.
Xanthoxylum	No. 30	Alcohol 3 vols.; Water 1 vol.	A.	850 mils.

List of Fluidextracts Standardized by Assay.

By Biological Assay:

Fluidextract of Aconite, Fluidextract of Cannabis, Fluidextract of Digitalis, Fluidextract of Squill.—U. S. P.

Fluidextract of Apocynum.—Nat. Form.

By Chemical Assay:

Gravimetrically: Fluidextract of Cinchona, Fluidextract of Colchicum Seed, Fluidextract of Guarana, Fluidextract of Hydrastis.—U. S. P.

Fluidextract of Cinchona (aqueous), Fluidextract of Colchicum Corm.—Nat. Form.

Volumetrically: Fluidextract of Aconite, Fluidextract of Belladonna Root, Fluidextract of Hyoscyamus, Fluidextract of Ipecac, Fluidextract of Nux Vomica, Fluidextract of Pilocarpus.—U. S. P.

Fluidextract of Conium, Fluidextract of Stramonium.—Nat. Form.

Fluidglycerates.—This name is applied in the *National Formulary* to a small number of concentrated solutions, intended to be of the same drug strength as fluidextracts. They are made with a menstruum composed of a mixture of glycerin and water, followed by chloroform water, and contain in the finished product 50 per cent., by volume of glycerin, but no alcohol. The drug is used in coarse, No. 20 or No. 30, powder, and is extracted by maceration, followed by percolation, after the manner directed for fluidextracts. Thus far the following fluid-glycerates have been introduced: Cascara Sagrada, Aromatic Cascara Sagrada, Glycyrrhiza, Krameria, and Rhubarb.

SPECIAL REMARKS.

Fluidextractum Aconiti (*Fluidextract of Aconite*).—This fluidextract is prepared by fractional percolation, as directed in Process C, because preparations of aconite are liable to deteriorate upon prolonged application of heat. The Pharmacopœia requires that it shall contain 0.005 Gm. of the ether-soluble alkaloids of aconite in each mil. (or Cc.) of the finished product, to be determined volumetrically by titration with tenth-normal sulphuric acid, and has fixed the limit of variation from the official standard at 10 per cent., namely, not less than 0.45 Gm. nor more than 0.55 Gm. of ether-soluble alkaloids in 100 mils. (or Cc.) of fluidextract.

Fluidextract of aconite may also be assayed biologically, in which case the minimum lethal dose should be not less than 0.0004 mil. (or Cc.) for each gram of body weight of the guinea-pig.

Fluidextractum Aspidospermatis (*Fluidextract of Aspidosperma*, also known as *Fluidextract of Quebracho*).—Since the bark of white quebracho only is officially recognized, the presence of red quebracho

bark must be avoided; it may be readily detected by treating shavings from the inner bark with alcohol, evaporating the tincture, boiling the residue with water and adding ferric chloride solution, when a green and not a brown color should be developed. Experience has shown that the official menstruum, containing about 62 per cent. of alcohol and 11 per cent. of glycerin, extracts the active principles of the drug, the fluidextract keeping well.

Fluidextractum Belladonnæ Radicis (*Fluidextract of Belladonna Root*).—As indicated in the title, this fluidextract should always be made from the root and should not be confounded with the commercial fluidextract of belladonna leaves. The Pharmacopœia requires that it shall contain 0.0045 Gm. of mydriatic alkaloids in each mil. (or Cc.) of the finished product, to be determined volumetrically by titration with tenth-normal sulphuric acid, and has fixed the limit of variation from the official standard at 10 per cent., namely, not less than 0.405 Gm. nor more than 0.495 Gm. of mydriatic alkaloids in 100 mils. (or Cc.) of fluidextract.

The liquid extract of belladonna root of the British Pharmacopœia is about 66 per cent. stronger than our preparation, containing 0.75 Gm. of mydriatic alkaloids in 100 mils. (or Cc.).

Fluidextractum Buchu (*Fluidextract of Buchu*).—As now made with strong alcohol, this preparation is of a rich green color and not miscible with water without precipitation.

Compound fluidextract of buchu, of the *National Formulary*, is made from a mixture of buchu, cubeb, juniper and uva ursi, of which the buchu constitutes more than 50 per cent. by weight.

Fluidextractum Cannabis (*Fluidextract of Cannabis*, also known as *Fluidextract of Hemp*).—The Pharmacopœia now recognizing both the American and Indian varieties of hemp under the official title Cannabis, the fluidextract may be made from either variety, but the name of the particular variety used should be indicated on the label, so as to enable physicians better to determine the relative value of the two preparations. The Pharmacopœia directs that fluidextract of cannabis shall be assayed biologically, the official standard being that not more than 0.03 mil. (or Cc.) of fluidextract per kilogram of body weight shall be required to produce incoördination when given to dogs.

As exposure to heat, except in a vacuum apparatus, appears to have a deleterious effect on preparations of cannabis, fractional percolation is likely to yield a better fluidextract than the official process.

Fluidextractum Cascaræ Sagradæ (*Fluidextract of Cascara Sagrada*).—Since boiling water has been found a most efficient solvent for the active principles of cascara bark, the official menstruum has been changed accordingly. After concentration of the aqueous percolate to three-fourths of the intended volume of finished fluidextract, one-third of its volume of official alcohol is added as a preservative, and the whole well mixed.

The present official title is more in keeping with commercial usage, the crude drug being better known as cascara sagrada bark, but the fluidextract may still occasionally be prescribed under the former official title, fluidextract of rhamnus purshiana.

Fluidextractum Cascaræ Sagradæ Aromaticum (*Aromatic Fluidextract of Cascara Sagrada*, also sometimes designated as *Aromatic, Bitterless, or Tasteless Cascara*).—The preliminary treatment of the cascara bark with one-eighth of its weight of calcined magnesia and about twice its weight of boiling water for two hours is for the purpose of removing the characteristic bitter taste of the drug; the mixture is then percolated with boiling water to exhaustion. After concentration of the aqueous percolate to one-half of the intended volume of finished fluidextract, pure extract of licorice is dissolved therein, and when cold, glycerin and an alcoholic solution of methyl salicylate and the oils of anise, cassia and coriander are added, partly as flavoring agents and partly as preservatives.

Fluidextractum Cinchonæ (*Fluidextract of Cinchona*, also known as *Fluidextract of Calisaya Bark*).—The addition of hydrochloric acid to the menstruum has been found to facilitate the extraction of the alkaloids and also to lessen the tendency to precipitation. The standard for alkaloidal content has been changed from 0.04 Gm. of anhydrous ether-soluble alkaloids to 0.05 Gm. of total alkaloids dried at 100° C. in each mil. (or Cc.) of fluidextract, to be determined gravimetrically. The limit of variation from the official standard has been fixed by the Pharmacopœia at 10 per cent., namely, not less than 4.5 Gms. nor more than 5.5 Gms. of total alkaloids in 100 mils. (or Cc.) of fluidextract.

Fluidextractum Colchici Seminis (*Fluidextract of Colchicum Seed*).—In order to free the drug from fatty matter, which has proved very objectionable in all its preparations, the powdered seed are percolated with purified petroleum benzin and then dried again before treatment with the hydroalcoholic menstruum. The Pharmacopœia requires that the fluidextract shall contain 0.004 Gm. of colchicine in each mil. (or Cc.), and has fixed the limit of variation from the official standard at 10 per cent., to be determined gravimetrically, namely, not less than 0.36 Gm. nor more than 0.44 Gm. of colchicine in 100 mils. (or Cc.) of fluidextract.

Fluidextractum Digitalis (*Fluidextract of Digitalis*, also known as *Fluidextract of Foxglove*).—Experience having shown that this fluidextract, when made with diluted alcohol, as heretofore, deteriorates when kept for some time, the alcoholic strength of the menstruum has been changed so as to contain about 84 per cent. of official alcohol, which the large manufacturers have found satisfactory. The efficiency of fluidextract of digitalis is determined biologically by its action on frogs; when thus tested, the minimum lethal dose should not be greater than 0.0006 mil. (or Cc.), or the equivalent in fluidextract of 0.0000005 Gm. of ouabain for each gram of body weight of the frog.

Fluidextractum Ergotæ (*Fluidextract of Ergot*).—The addition of 2 per cent. of official hydrochloric acid to diluted alcohol improves the menstruum by insuring more complete extraction of the active constituents of the drug and also prevents any loss during evaporation of the weak percolate. Although ergot is known to contain a considerable amount of fixed oil, no provision is made for its removal.

Fluidextractum Frangulæ (*Fluidextract of Frangula*, also known as *Fluidextract of Buckthorn Bark*).—Like cascara sagrada, buckthorn bark is readily extracted by percolation with boiling water; in fact this menstruum has been found better than a mixture of alcohol and water. After concentration of the aqueous percolate to three-fourths of the intended volume of finished fluidextract, one-third of its volume of official alcohol is added as a preservative and the whole well mixed.

Fluidextractum Glycyrrhizæ (*Fluidextract of Glycyrrhiza*, also known as *Fluidextract of Licorice*).—The use of an alkaline menstruum, consisting of a mixture of chloroform water 27 volumes and official ammonia water 3 volumes, is necessary for complete extraction of the sweet principle of licorice root, which is present in the drug partly in an insoluble form, but combines with ammonia and becomes soluble. Chloroform water is preferable to plain water, since it prevents fermentation liable to occur during the process. The aqueous solution, after solution of the soft extract in the reserve portion, having been brought up to three-fourths of the intended volume of the finished fluidextract, is mixed with one-third of its volume of official alcohol and set aside for a week to allow precipitation of mucilaginous and other inert matter, after which it is filtered, the precipitate being washed with a mixture of alcohol 1 volume and water 3 volumes.

Fluidextractum Granati (*Fluidextract of Pomegranate*).—The menstruum directed by the Pharmacopœia contains 10 per cent. by volume of glycerin and is of the same alcoholic strength as diluted alcohol. It appears to extract the alkaloidal constituents of the drug perfectly and the finished fluidextract keeps well.

Fluidextractum Guaranæ (*Fluidextract of Guarana*).—The present official menstruum is about 50 per cent. stronger in alcohol than that formerly directed. The Pharmacopœia requires that fluidextract of guarana shall contain 0.04 Gm. of caffeine in each mil. (or Cc.) to be determined gravimetrically, and the limit of variation from the official standard has been fixed at 10 per cent., namely, not less than 3.6 Gms. nor more than 4.4 Gms. of caffeine in 100 mils. (or Cc.) of fluidextract.

Fluidextractum Hydrastis (*Fluidextract of Hydrastis*, also known as *Fluidextract of Golden Seal*).—The Pharmacopœia requires that this fluidextract shall contain 0.02 Gm. of the ether-soluble alkaloids of hydrastis in each mil. (or Cc.), to be determined gravimetrically, and has fixed the limit of variation from the official standard at 10 per cent., namely, not less than 1.8 Gms. nor more than 2.2 Gms. of ether-soluble alkaloids in 100 mils. (or Cc.) of fluidextract.

Fluidextractum Hyoscyami (*Fluidextract of Hyoscyamus*, also known as *Fluidextract of Henbane*).—The Pharmacopœia requires that this fluidextract shall contain 0.00065 Gm. of mydriatic alkaloids in each mil. (or Cc.), to be determined volumetrically by titration with tenth-normal sulphuric acid, and has fixed the limit of variation from the official standard at slightly over 15 per cent., namely, not less than 0.055 Gm. nor more than 0.075 Gm. of mydriatic alkaloids in 100 mils. (or Cc.) of fluidextract.

Fluidextractum Ipecacuanhæ (*Fluidextract of Ipecac*).—The object of adding diluted hydrochloric acid to the menstruum for this fluidextract is to facilitate the extraction of the alkaloids, emetine and cephæline, while permitting the use of a weaker alcoholic liquid; the alkaloids are kept in solution as hydrochlorides. The Pharmacopœia requires that fluidextract of ipecac shall contain 0.02 Gm. of ether-soluble alkaloids in each mil. (or Cc.), to be determined volumetrically by titration with tenth-normal sulphuric acid, and has fixed the limit of variation from the official standard at 10 per cent., namely, not less than 1.8 Gms. nor more than 2.2 Gms. of ether-soluble alkaloids in 100 mils. (or Cc.) of fluidextract.

Fluidextractum Lobeliæ (*Fluidextract of Lobelia*).—On account of the volatile nature of the active principle of lobelia, an acid menstruum, consisting of diluted alcohol containing 5 per cent. by volume of official acetic acid, is employed, whereby the extraction of the alkaloid is facilitated and loss prevented during evaporation of the weak percolate. The strongly acid menstruum directed by the last Pharmacopœia, containing 27.5 of official acetic acid, yielded an efficient fluidextract, which, however, was unpopular on account of its very acid character.

Fluidextractum Nucis Vomicæ (*Fluidextract of Nux Vomica*).—The official requirement for alkaloidal content of this fluidextract has been completely changed from a definite strychnine content to a definite content of total alkaloids, which must be 0.025 Gm. in each mil. (or Cc.) of the finished product, to be determined volumetrically by titration with tenth-normal sulphuric acid. The Pharmacopœia has fixed the limit of variation from the official standard at 5 per cent., namely, not less than 2.37 Gms. nor more than 2.63 Gms. of total alkaloids in 100 mils. (or Cc.) of fluidextract.

Since the official powdered extract of nux vomica contains 16 per cent. of total alkaloids, a small quantity of the fluidextract may be conveniently prepared extemporaneously by triturating 1.6 Gm. of the powdered extract with 10 mils. (or Cc.) of a mixture of alcohol 3 volumes and water 1 volume for some time in a glass mortar and then filtering the mixture; 1.6 Gm. of the official powdered extract of nux vomica should contain 0.256 Gm. of total alkaloids, which is the quantity required for 10 mils. (or Cc.) of the fluidextract.

Fluidextractum Pilocarpi (*Fluidextract of Pilocarpus*, also known as *Fluidextract of Jaborandi*).—The official requirement for alkaloidal

content of this fluidextract has been increased 50 per cent. over that formerly demanded, the present standard being 0.006 Gm. of alkaloids in each mil. (or Cc.) of the finished product. The Pharmacopœia has fixed the limit of variation from the official standard at nearly 8.5 per cent., namely, not less than 0.55 Gm. nor more than 0.65 Gm. of alkaloids in 100 mils. (or Cc.) of fluidextract.

Fluidextractum Podophylli (*Fluidextract of Podophyllum*, also known as *Fluidextract of Mayapple or Mandrake*).—Since the medicinal value of the drug resides wholly in its resinous constituents, alcohol is a better menstruum for the preparation of the fluidextract than the mixture of alcohol and water formerly used.

Fluidextractum Rhei (*Fluidextract of Rhubarb*).—Although rhubarb will yield its active virtues to diluted alcohol, and even to water alone, the strongly alcoholic menstruum directed for the fluidextract, first suggested by Alonzo Robbins about 1884, has, after numerous experiments, been found necessary to prevent gelatinization and precipitation.

Fluidextractum Sabal (*Fluidextract of Sabal*, also known as *Fluidextract of Saw Palmetto Berries*).—The strongly alcoholic menstruum directed by the Pharmacopœia for this fluidextract is necessary on account of the oily and resinous constituents of the drug.

Fluidextractum Sarsaparillæ Compositum (*Compound Fluidextract of Sarsaparilla*).—There appears to be no good reason why the sarsaparilla and licorice root should be used in coarse powder, while the sassafras and mezereum are ordered in finer powder. The sarsaparilla constitutes 75 per cent. of the drugs ordered, and in the author's experience a uniform powder of all four drugs, of No. 30 fineness, yields very satisfactory results with such quantities as are directed in the official formula. Owing to the ligneous character of the drugs, firm packing has been found desirable.

Fluidextractum Scillæ (*Fluidextract of Squill*).—The drug in coarse powder is best exhausted by alternate maceration and percolation with a menstruum containing about 66 per cent. of official alcohol. The resulting tincture is concentrated to about one-sixth of its volume and treated with two and one-half times its volume of alcohol, whereby mucilaginous and saccharine matters are removed, the medicinally active principles (consisting of glucosides) remaining in solution. After decanting and filtering the supernatant liquid, the syrupy residue is washed with 2 successive portions of a mixture of alcohol 4 volumes and water 1 volume, the washings being also passed through the filter. Finally the filtrate is evaporated to four-fifths of the intended volume of finished fluidextract and brought up to the required volume by addition of diluted alcohol.

The Pharmacopœia requires that if fluidextract of squill be assayed biologically, the minimum lethal dose should not be greater than 0.006 mil. (or Cc.), or the equivalent in fluidextract of 0.0000005 Gm. of ouabain, for each gram of body weight of the frog.

Fluidextractum Senegæ (*Fluidextract of Senega*).—The addition of ammonia water to the solution of the soft extract in the reserve percolate is for the purpose of forming soluble compounds with the pectin principles present, and thus prevent gelatinization of the fluidextract. It is very questionable whether ammonia, on account of its volatile nature and easy dissociation of its compounds, is preferable to solution of potassium or sodium hydroxide.

Fluidextractum Sennæ (*Fluidextract of Senna*).—While the menstruum directed, diluted alcohol, will extract all the medicinal virtues of senna leaves and keep them in solution, the present fluidextract is apt to cause more unpleasant griping than that of the last Pharmacopœia, in which the disturbing resinous principles were first removed by percolation with strong alcohol.

Fluidextractum Staphisagriæ (*Fluidextract of Staphisagria*, also known as *Fluidextract of Stavesacre*).—Since stavesacre seed contain from 20 to 30 per cent. of fixed oil, the latter will be taken up by the strongly alcoholic menstruum and separate in the freshly prepared fluidextract. It may be removed by chilling and filtering, or by decantation and subsequent filtration of the fluidextract after addition of some purified talcum.

Fluidextractum Stillingiæ (*Fluidextract of Stillingia*, also known as *Fluidextract of Queen's Root*).—When made with diluted alcohol, this fluidextract sometimes gelatinizes on standing, which may be avoided either by using a menstruum richer in alcohol (alcohol 2 volumes and water 1 volume), or by adding sugar to the extent of 10 or 12 per cent. of the weight of the drug.

The compound fluidextract of stillingia of the *National Formulary* is made from a mixture of stillingia, corydalis, iris, sambucus, chimaphila, coriander and xanthoxylum berries, of which the stillingia and corydalis together represent 50 per cent.

Fluidextractum Taraxaci (*Fluidextract of Taraxacum*, also known as *Fluidextract of Dandelion*).—The addition of sodium hydroxide solution to the fluidextract, ordered by the last Pharmacopœia, seemed quite unnecessary and very properly has been dropped. This fluidextract is apt to precipitate for some time and the addition of 10 per cent. of glycerin to the menstruum is thought to diminish this tendency.

Fluidextractum Tritici (*Fluidextract of Triticum*, also known as *Fluidextract of Couch Grass*).—Although the Pharmacopœia directs percolation with boiling water to exhaustion, digestion of the finely cut drug will be found equally useful in every way; the operation to be repeated once or twice, as may be necessary. The infusion should then be rapidly concentrated, and when cold mixed with the alcohol and set aside for forty-eight hours, whereby mucilaginous and albuminous matter is separated. The finished product contains 20 per cent. of alcohol, which protects the saccharine liquid against fermentation.

Fluidextractum Veratri Viridis (*Fluidextract of Veratrum Viride,* also known as *Fluidextract of Green Hellebore*).—The Pharmacopœia no longer recognizes both the green and white varieties of veratrum under the official title of the drug, and hence the title of the official fluidextract has again been changed to that in use prior to the previous revision.

Fluidextractum Xanthoxyli (*Fluidextract of Xanthoxylum,* also known as *Fluidextract of Prickly Ash Bark*).—Since the Pharmacopœia recognizes both commercial varieties of prickly ash bark, the northern and southern, under the official title Xanthoxylum, the fluidextract may be made from either bark or from a mixture of the two. Prickly ash berries are not recognized in The Pharmacopœia, but enter into the composition of compound fluidextract of stillingia of the *National Formulary.*

The formulas for the remaining fluidextracts of the Pharmacopœia appear to yield satisfactory results and do not call for special comment.

CHAPTER XXIII.

EXTRACTS.

EXTRACTS are permanent, solid or semisolid preparations, obtained by evaporation of a solution of the medicinal principles of drugs. These solutions are prepared, as a rule, in the manner already explained under Fluidextracts, the solvents or menstrua employed being either water, water and alcohol, alcohol, or ether. According to the different menstrua used in their manufacture, extracts are divided into *aqueous hydro-alcoholic, alcoholic,* and *ethereal,* the last-named class being recognized in the Pharmacopœia under the name of *oleoresins.*

For aqueous extracts cold water is preferred both in this country and abroad, and has been found to yield superior products. While hot water increases the yield of extractive matter, it is objectionable because it carries into the solution starch and other inert matter; in a few instances digestion is, however, still employed. In the preparation of aqueous extracts the solution is freed from objectionable matter, whenever necessary, by heating to the boiling point and straining before final evaporation. In the case of alcoholic or hydro-alcoholic extracts, where the solution of active constituents is invariably obtained by percolation, it would seem desirable to set aside the first third of the percolate as a reserve, to be incorporated with the weaker percolate when this has been evaporated to the consistence of a syrupy fluid. The recovery of alcohol is effected, as a rule, by distillation in a suitable still, the final concentration being conducted in porcelain dishes with constant stirring, so as to insure a homogeneous mass and prevent the separation of resinous and other matter. As the concentration approaches the condition of a thick syrup, continuous stirring is also necessary to prevent the formation of a film, which becoming gradually thicker, retards evaporation of moisture and consequently causes accumulation of heat within the mass, to the possible injury of some of the constituents. In large manufacturing establishments concentration of the solution is generally conducted in a vacuum apparatus and mechanical stirrers are conveniently operated by steam, electric, or water motors. Metallic stirrers should never be employed, only those of porcelain, glass or wood being permissible. To guard against the separation of coloring matter or changes in other constituents of the solution, concentration should be effected on a waterbath at a temperature not exceeding 60° C. (140° F.) (70° C., U. S. P.), if a vaccuum apparatus is not available.

In fresh plants the solution of the medicinal principle is represented by the juice, and may be obtained by expression; extracts prepared

by simple evaporation of the fresh juice of a plant are known as inspissated juices. The U. S. Pharmacopœia does not recognize inspissated juices, since the narcotic herbs which are used in Europe for this purpose are not indigenous in the United States. The juice is obtained from the fresh plant, after removal of extraneous matter, by bruising in a stone mortar with the aid of a hard wood pestle until reduced to a smooth pulpy mass, which is then strongly expressed in canvas bags; in order to recover all the juice, the residue is often mixed with water and again expressed. When the plant is not sufficiently moist to enable the formation of a soft pulp, water is sprinkled over it from time to time.

Besides the medicinal principles, the expressed juices of fresh herbs contain also mucilaginous and albuminous matter in solution and variable quantities of chlorophyl or green coloring-matter in suspension; of these, the albuminous principles are most objectionable, as upon concentration of the juice they undergo change and are likely to render the finished extract tough and insoluble. When roots are expressed, as in the case of the corm of colchicum, starch, which is present in the juice in place of chlorophyl, passes through the press-cloth, and must be removed by subsidence and decantation.

Consistence of Extracts.—The U. S. Pharmacopœia recognizes three kinds of solid extracts, those of a soft, semiliquid consistence, like thick honey, those of pilular consistence, and those evaporated to complete dryness. A pilular consistence is such a condition as will allow the extract to be rolled into masses of pilular form without adhering to the fingers or subsequently losing shape; this is rarely met with in the market, except in the case of former British narcotic extracts which derived their firmness chiefly from the chlorophyl and gummy matter present. Pilular consistence for the extracts made in this country, by the official formulas, is practically unattainable at all seasons, for extracts made in summer are likely to become too hard in winter, while those evaporated to the proper consistence in winter are prone to soften in summer. Some extracts become tough and hard in the course of time; these are best retained in proper condition by incorporating with them, while still warm, 5 per cent. of their weight of glycerin. The condition of complete dryness is not applicable to all extracts, but can be readily maintained for all those so directed by the Pharmacopœia, provided heat and moisture be excluded.

Powdered extracts are made by a more complete evaporation of the solution obtained by percolation, the latter having been prepared with a menstruum that will extract the active principles of the drug with a minimum amount of inert matter; when the drug contains fatty constituents, as in the case of calabar bean, colchicum corm, ergot, nux vomica, etc., it is necessary to provide for their removal by appropriate means, since their presence will interfere with a satisfactory pulverulent condition, and for this purpose treatment with purified petroleum benzin is officially directed.

A soft mass having been obtained, it is spread on plates of tinned metal or of glass and desiccation effected either in specially constructed

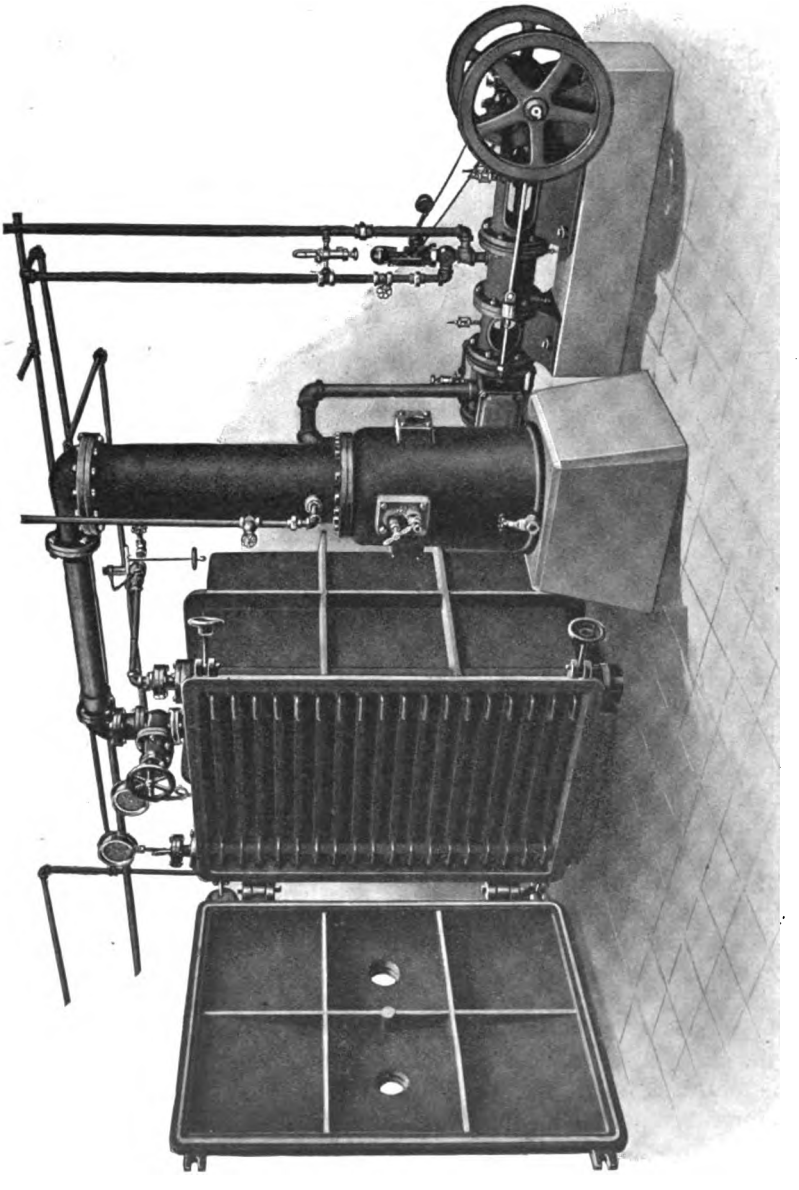


Fig. 227.—Complete vacuum shelf dryer with condenser.

vacuum dryers, such as shown in Figs. 227 and 228, or by means of currents of warm air. Finally the dry extract is reduced to powder in pebble mills, whereby heat and agglutination are avoided. The

pulverent condition is maintained by addition of some inert substance, such as dried starch or a mixture of dried starch and magnesia.

The vacuum shelf dryer shown in Fig. 227 is used in nearly all large manufacturing establishments of the present day. It consists of a square or rectangular chamber containing hollow steam or hot water heated shelves, placed one above the other, the space between the shelves varying from 2.5 to 4 inches. The chamber has a door at one or both ends for unloading purposes. The material to be dried having been loaded in trays or pans, is placed on the shelves; the apparatus is then closed up, the vacuum produced and the drying commenced. If desired, the volatile matter or solvents removed from the material, which in some instances is valuable, may be reclaimed.

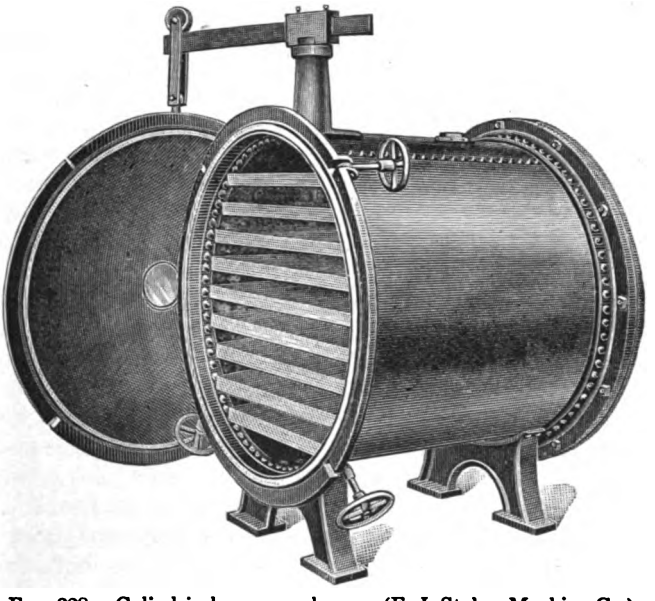


FIG. 228.—Cylindrical vacuum dryer. (F. J. Stokes Machine Co.)

Powdered extracts are liable to absorb moisture from the atmosphere and should therefore be preserved in tightly stoppered wide-mouthed bottles in a cool, dry place. The advantage of powdered extracts for dispensing purposes is self-evident, and lies in the fact that they can be more accurately weighed and more easily incorporated with a mixture of other medicinal substances.

The Abstracts of the U. S. Pharmacopœia for 1880 were closely allied to the present powdered extracts. They were much weaker preparations, being made to represent twice their weight of crude drug. The general plan for preparing abstracts was to make a fluid-extract of the drug with strong alcohol, to mix this with some sugar of milk, dry by spontaneous evaporation in a warm place, then add

sufficient sugar of milk to bring the product up to one-half the weight of the powdered drug used, and finally reduce to a fine powder.

Aqueous Extracts.—While the use of hot (boiling) water for exhaustion of the drug in some cases increases the yield of extract, by bringing into solution starch and other inert matter, it more frequently injures the quality of the product by inducing changes in certain principles which do not occur by infusion at ordinary temperatures. There is but one instance, that of extract of logwood, in which the *National Formulary* directs extraction by boiling, and this is on account of the difficulty of exhausting the tough wood. In Europe, digestion is still preferred for a few aqueous extracts, but, as a rule, maceration and percolation with cold water have been found to yield superior extracts. For the better extraction of the active virtues of the drug, an addition of acid or alkali is sometimes made, as in the case of the official extract of colchicum corm and pure extract of glycyrrhiza. In the preparation of aqueous extracts the solution is freed from objectionable matter, whenever necessary, by heating to the boiling point and straining before final evaporation.

Alcoholic and Hydro-alcoholic Extracts.—For these two classes of extracts percolation is decidedly the best method of extracting the medicinal principles of the drugs, the operation being continued to complete exhaustion. If percolation be conducted at the rate of 5 drops per minute, from 3 to 4 mils. (or Cc.) of percolate should suffice for each Gm. of drug. In many cases, particularly those of the mydriatic drugs, the active principles of which are easily split up by prolonged application of heat, it is very desirable to set aside the first third of the percolate as reserve, to be incorporated with the remainder when this has been reduced to the condition of a syrupy fluid. The recovery of the alcohol is effected, as in the case of fluidextracts, by distillation in a suitable still, the final evaporation being conducted in porcelain dishes, with constant stirring, so as to insure a homogeneous mass and prevent the separation of resinous and other matter.

Changes by Evaporation.—All plants contain one or more principles, which, though originally colorless, are very easily altered under the influence of air and heat, acquiring a yellow or brown color. It is not known whether the so-called *colorless extractive* is alike in all plants, neither is its composition or the nature of the changes produced under the conditions mentioned known, except that the heat of boiling water and the prolonged action of oxygen will convert it ultimately into a blackish insoluble substance, to which the name *apotheme* has been given, and which appears to be allied to *humin*. Extractive is almost insoluble in absolute alcohol and ether, but dissolves freely in weaker alcohol and water, and is removed from its solution by animal charcoal and aluminum hydroxide, the more readily after it has become colored by oxidation. It is with difficulty freed from admixtures, and the terms sweet, bitter, acrid, etc., as applied to extractives, refer to the same body in a more or less altered condition, combined or intimately mixed with other principles to which the peculiar taste is due. The

injurious influence of air and heat upon the vegetable juices is mainly confined to the alterations of this extractive, and extends, in a limited degree only, to the majority of the well defined principles. Its effects have often been much overrated, except as regards the appearance of the extracts. The color of the different extracts varies with the nature of the drug from which they have been made, but should never be black. The characteristic taste, and to some extent also the odor of the drug, should be perceived in its extract, and it should yield a nearly clear or moderately turbid solution with the menstruum used in its preparation.

Classification of Extracts.—The Pharmacopœia and the *National Formulary* together give directions for the preparation of 39 extracts, of which number 37 may be classified according to the menstruum used for extraction of the respective drugs, as follows:

Made with alcohol:

Extract of Aconite (with addition of tartaric acid), Extract of Belladonna Leaves (powdered), Extract of Cannabis, Extract of Cimicifuga, Extract of Colchicum Corm, Extract of Gelsemium, Extract of Hydrastis (with addition of tartaric acid), Extract of Oxgall, Extract of Physostigma (with addition of tartaric acid), Extract of Rhubarb, Extract of Stramonium (powdered).—U. S. P.

Extract of Jalap.—Nat. Form.

Made with a mixture of alcohol 8.5 volumes, and water 1.5 volume:

Extract of Ergot (with addition of hydrochloric acid).—U. S. P.

Made with a mixture of alcohol 4 volumes, and water 1 volume:

Extract of Sumbul.—U. S. P.

Extract of Euonymus, Extract of Podophyllum.—Nat. Form.

Made with a mixture of alcohol 3 volumes, and water 1 volume:

Extract of Belladonna Leaves (pilular), Extract of Hyoscyamus, Extract of Nux Vomica, Extract of Stramonium (pilular).—U. S. P.

Extract of Cinchona, Extract of Ignatia, Extract of Leptandra.—Nat. Form.

Made with diluted alcohol:

Extract of Colocynth, Extract of Viburnum Prunifolium.—U. S. P.

Extract of Conium.—Nat. Form.

Made with a mixture of alcohol 1.25 volumes, and water 8.75 volumes.

Extract of Taraxacum.—U. S. P.

Made with boiling water:

Extract of Cascara Sagrada.—U. S. P.

Extract of Aloes, Extract of Hematoxylon.—Nat. Form.

Made with chloroform water:

Extract of Ergot (aqueous).—Nat. Form.

Made with cold water:

Extract of Gentian, Extract of Glycyrrhiza, pure, (with addition of ammonia water), Extract of Malt (followed by warm water), Extract of Opium.—U. S. P.

Extract of Quassia.—Nat. Form.

Extract of Apples (ferrated) and Extract of Colocynth (compound) cannot be classified, as they are not made by extraction of drugs.

The following extracts are recognized either in the Pharmacopœia or the *National Formulary:*

Pilular Extracts.	Extract of Belladonna Leaves, Extract of Cannabis, Extract of Ergot, Extract of Gentian, Extract of Glycyrrhiza (pure), Extract of Hyoscyamus, Extract of Stramonium, Extract of Sumbul, Extract of Taraxacum.—U. S. P.
	Extract of Apples (ferrated), Extract of Cinchona, Extract of Conium, Extract of Ergot (aqueous), Extract of Jalap, Extract of Podophyllum.—Nat. Form.
Powdered Extracts.	Extract of Aconite, Extract of Belladonna Leaves, Extract of Cascara Sagrada, Extract of Cimicifuga, Extract of Colchicum Corm, Extract of Colocynth, Extract of Colocynth (compound), Extract of Gelsemium, Extract of Hydrastis, Extract of Nux Vomica, Extract of Opium, Extract of Oxgall, Extract of Physostigma, Extract of Rhubarb, Extract of Stramonium, Extract of Viburnum Prunifolium.—U. S. P.
	Extract of Aloes, Extract of Euonymus, Extract of Ignatia, Extract of Krameria, Extract of Leptandra, Extract of Quassia.—Nat. Form.
Soft Extracts.	Extract of Malt.—U. S. P.
Dry Extracts.	Extract of Hæmatoxylon.—Nat. Form. (This extract is not directed to be in powdered form.)

For the purpose of insuring greater uniformity in the quality of pilular as well as powdered extracts, standardization is resorted to in a majority of cases, based either on a definite percentage content of alkaloid or on a definite relation of the weight of finished extract to the weight of drug from which it is made. This necessitates the addition of a suitable diluent and the Pharmacopœia and *National Formulary* both direct glucose as a diluent in the case of pilular extracts, and dried starch for powdered extracts; for the latter, they also permit the use of sugar of milk, powdered licorice root, magnesium carbonate, or the finely powdered drug or marc from which the extract was made.

The following are the standardized extracts of the Pharmacopœia and the *National Formulary:*

Based on Definite Content of Alkaloid.

Extract of Aconite (2 per cent.), Extract of Belladonna Leaves, Pilular and Powdered (1.25 per cent.), Extract of Colchicum Corm (1.4 per cent.), Extract of Hydrastis (10 per cent.), Extract of Hyoscyamus (0.25 per cent.), Extract of Nux Vomica (16 per cent.), Extract of Opium (20 per cent.), Extract of Physostigma (1.95 per cent.), Extract of Stramonium, Pilular and Powdered (1 per cent.).—U. S. P.

Extract of Cinchona (24 per cent.), Extract of Conium (2 per cent.), Extract of Ignatia (6 per cent.).—Nat. Form.

Based on Relation of Weight of Extract to Weight of Drug Used.

Extract of Cascara Sagrada (1 to 3), Extract of Cimicifuga (1 to 4), Extract of Colocynth (1 to 4), Extract of Gelsemium (1 to 4), Extract of Oxgall (1 to 8), Extract of Rhubarb (1 to 2) Extract of Viburnum Prunifolium (1 to 5).—U. S. P.

Extract of Aloes (1 to 2), Extract of Euonymus (1 to 4), Extract of Krameria (1 to 4), Extract of Leptandra (1 to 4), Extract of Quassia (1 to 10).—Nat. Form.

SPECIAL REMARKS.

Extractum Aconiti (*Extract of Aconite*).—The addition of a small quantity of tartaric acid, ½ per cent., to the alcoholic menstruum is intended to facilitate the extraction of the alkaloids. After the percolate has been evaporated to a syrupy consistence, it is treated with two successive portions of purified petroleum benzin to remove fatty matter, which would interfere with the subsequent pulverization of the extract; dried starch is then added and the mixture thoroughly dried, powdered and weighed. Having assayed a small portion of the powdered extract, sufficient dried starch is added, so that the finished product contains 2 per cent. of ether-soluble alkaloids.

The necessary quantity of dried starch to be added may be determined as follows: Suppose the powdered extract is found to contain, by assay, 2.36 per cent. of ether-soluble alkaloids, then each gram contains 0.0236 Gm., instead of 0.02 Gm. the prescribed standard, and will therefore require the addition of 0.18 Gm. of dried starch, for $0.02 : 0.0236 :: 1 : x$ ($x = 1.18$), where x represents the weight of official extract that corresponds to 1 Gm. of the assayed extract; then $1.18 - 1 = 0.18$. This method of calculation can also be applied to other extracts, pilular or powdered.

The Pharmacopœia requires that powdered extract of aconite, when assayed chemically, shall yield not less than 1.8 per cent. nor more than 2.2 per cent. of the ether-soluble alkaloids of aconite, to be determined by titration with tenth-normal sulphuric acid, and if assayed biologically, the minimum lethal dose should be not greater than 0.00001 Gm. for each gram of body weight of the guinea-pig. One Gm. of the extract represents about 4 Gms. of aconite.

Extractum Aloes (*Extract of Aloes*).—Since no special variety of aloes is designated by the *National Formulary*, the extract may be made from any one of the three varieties recognized under the official title Aloe, but it is probable that Curacao aloes, frequently called Barbadoes aloes, is chiefly employed. The large proportion of boiling water ordered by the *National Formulary* is for the purpose of avoiding the admixture of resin; a concentrated aqueous solution of aloes retains in solution much of the resin present, whereas a dilute solution deposits it on cooling.

The Pharmacopœia states that Socotrine aloes yields not less than 50 per cent. of its weight to cold water, whereas Curacao and Cape aloes both yield not less than 60 per cent.; hence there seems to be little or no occasion for the addition of dried starch to produce a powdered extract representing twice its weight of the drug from which it is made. Extract of aloes, especially without the addition of starch, is apt to be affected by hot weather and should, therefore, be kept in a cool place.

Extractum Belladonnæ Foliorum (*Extract of Belladonna Leaves*).—The official title of this extract is rarely used by physicians, the more

familiar term *Extractum Belladonnæ* being employed in prescription writing. Both a pilular and a powdered extract of belladonna leaves are recognized, which are of the same alkaloidal strength and represent about four times their weight of the leaves. The official standard is 1.25 per cent. of mydriatic alkaloids, glucose being used as a diluent for the pilular extract and dried starch for the powdered extract. The necessary amount of diluent to be used may be ascertained by calculation, as indicated under Extract of Aconite (see above). Extract of belladonna of the British Pharmacopœia is 20 per cent. weaker in alkaloid content, while those of the German and Swiss Pharmacopœias are 20 per cent. stronger; all three extracts are made from the leaves and are of pilular consistence.

The Pharmacopœia requires that extract of belladonna leaves, when assayed, shall yield not less than 1.18 per cent., nor more than 1.32 per cent., of mydriatic alkaloids, to be determined by titration with tenth-normal sulphuric acid.

Extractum Cannabis (*Extract of Cannabis*).—The Pharmacopœia having admitted both American-grown and Indian hemp under the title Cannabis, the old title Extract of Indian Hemp has been dropped. The extract may be made from either variety of the drug, but it would seem desirable that the particular one used be indicated on the label, especially if comparative tests of efficiency are to be made. The evaporation of the percolate should, if possible, be conducted in a vacuum apparatus, since the constituents of cannabis are easily affected by higher temperature and exposure to air. The average yield of extract is about 12 per cent.

The Pharmacopœia states that extract of cannabis, when assayed biologically, produces incoördination when administered to dogs in a dose of not more than 0.004 Gm. of extract per kilogram of body weight.

The extract is rich in resin, has a blackish-green color, and a peculiar, rather unpleasant heavy odor. It is soluble in alcohol, ether, chloroform, oil of turpentine, and fixed oils. Its alcoholic solution is precipitated by solution of potassium or sodium hydroxide, the resin being insoluble in alkalies.

While chiefly administered in pill form, extract of cannabis is sometimes prescribed in mixtures and can then be best kept in suspension by dissolving it in a small quantity of expressed oil of almond and emulsifying the solution with the aid of acacia.

Extractum Cascaræ Sagradæ (*Extract of Cascara Sagrada*).—Hot (boiling) water has been found preferable to cold water for extraction of the medicinal principles of the bark, and the dry residue obtained by evaporation of the aqueous percolate is easily reduced to powder, and kept so by the addition of a mixture of calcined magnesia and starch. Cascara Sagrada will yield from 20 to 25 per cent. of dry extract when extracted with water, hence the official product is adjusted to represent three times its weight of the bark.

Extractum Cimicifugæ (*Extract of Cimicifuga*).—Since the residue obtained by evaporation of fluidextract of cimicifuga consists wholly of resinous matter, it is admirably adapted to the pulverulent form, which is easily maintained by the addition of finely powdered dried starch. The Pharmacopœia directs that the powdered extract shall represent four times its weight of the crude drug.

Extractum Cinchonæ (*Extract of Cinchona*).—This extract, of pilular consistence, is made with a menstruum composed of alcohol, 3 volumes, and water, 1 volume, and is required by the *National Formulary* to yield, when assayed gravimetrically, not less than 22 per cent., nor more than 26 per cent. of the total aklaloids of cinchona.

Extractum Colchici Cormi (*Extract of Colchicum Corm*).—The former acetous pilular extract of colchicum corm, official for many years, has been replaced by a powdered extract. Since alcohol is used as a menstruum for extracting the alkaloid, removal of the fatty matter becomes necessary, since its presence would interfere with perfect pulverization; this is accomplished by means of purified petroleum benzin in the same manner as indicated under Extract of Aconite (see p. 345). The residue having been mixed with some starch, is dried, powdered, weighed and assayed, and sufficient dried starch added so that the finished product shall contain 1.4 per cent. of colchicine.

The Pharmacopœia requires that powdered extract of colchicum corm, when assayed, shall yield not less than 1.25 per cent., nor more than 1.55 per cent. of colchicine, to be determined gravimetrically.

Extractum Colocynthidis (*Extract of Colocynth*).—In order to avoid the fixed oil which is present in the seeds, the Pharmacopœia directs that only the pulp of the colocynth shall be used. The hydro-alcoholic percolate obtained by the official formula is easily reduced to powder, and having been weighed is directed to be mixed with sufficient dried starch so that the finished product shall represent four times its weight of the crude drug from which it was made. This may not always be possible, since good colocynth pulp has been known to yield as much as 40 per cent. of dry extract when treated with diluted alcohol.

Extractum Colocynthidis Compositum (*Compound Extract of Colocynth*).—It is questionable whether as uniform a powder can be obtained by simply triturating the ingredients together, as was possible by the former official process. The finished product contains one-half of its weight of aloes, 16 per cent. of extract of colocynth, 15 per cent. of powdered soap, 14 per cent. of resin of scammony, and 5 per cent. of powdered cardamom seed.

Extractum Conii (*Extract of Conium*).—The *National Formulary* directs that the drug shall be extracted with diluted alcohol, the first percolate being reserved; having added diluted hydrochloric acid to the remainder of the percolate, this is evaporaed at a moderate temperature, incorporated with the reserve tincture and the whole evaporated to a pilular consistence. The finished extract contains 2 per cent.

of coniine, and when assayed by titration with tenth-normal sulphuric acid should yield not less than 1.8 per cent., nor more than 2.2 per cent. of the alkaloid.

Extractum Ergotæ (*Extract of Ergot*).—The Pharmacopœia directs that the powdered ergot be first deprived of the considerable quantity of oil present, by percolation with purified petroleum benzin, after which it is dried and extracted with a strongly alcoholic menstruum (alcohol, 85 volumes; water, 15 volumes) containing hydrochloric acid. The acid is added to facilitate the extraction of the alkaloids and to prevent loss of the same during evaporation of the percolate to a pilular consistence.

The Aqueous Extract of Ergot of the *National Formulary* is made by extracting powdered ergot with chloroform water; after concentration of the percolate, alcohol is added and the mixture set aside for several days to remove mucilaginous and other impurities. After filtration, the filtrate is evaporated to a pilular consistence at a moderate temperature. This purified aqueous extract of ergot seems better suited for hypodermic injection than the pharmacopœial preparation.

Extractum Euonymi (*Extract of Euonymus*).—Euonymus or wahoo bark is rich in resins and the *National Formulary* therefore directs a strongly alcoholic menstruum for extraction of the drug. The percolate is evaporated to dryness, powdered, weighed, and mixed with sufficient dried starch so that the finished product shall represent four times its weight of the crude drug.

Extractum Ferri Pomatum (*Ferrated Extract of Apples*).—This preparation, also known as *Crude Malate of Iron*, is made by macerating reduced iron with freshly expressed juice of apples, and heating on a waterbath until gas is no longer given off, adding water from time to time. After several days of rest, the liquid is filtered and evaporated to a pilular consistence.

Extractum Fellis Bovis (*Extract of Oxgall*).—This extract is intended to replace the purified oxgall formerly official, and is directed to be in powder form for greater convenience in dispensing. It is mixed with sufficient dried starch to represent eight times its weight of fresh oxgall. The alcohol extracts all the valuable constituents of the bile and prevents solution of the inert principles.

Extractum Gelsemii (*Extract of Gelsemium*).—The prescribed menstruum, alcohol, no doubt extracts all the medicinal properties of the drug. After reduction of the percolate to a soft extract, magnesium oxide and starch are added to facilitate drying and powdering; having weighed the powdered extract, sufficient dried starch is added so that the finished product shall represent four times its weight of the crude drug.

Extractum Gentianæ (*Extract of Gentian*).—All of the valuable bitter, principles of gentian are soluble in cold water, while much inert matter is avoided by the use of this menstruum; when hot water is employed, the yield of extract is vastly increased on account of the

large quantity of pectin compounds taken up. The ojbect of boiling the cold-water percolate, as directed in the U. S. Pharmacopœia, is to coagulate the albuminous matter, after removal of which the extract obtained forms an almost clear solution with water. With cold water, gentian yields about 30 per cent. of extract, which can be increased to 50 or 60 per cent. with hot water; the United States, German, French, and Swiss Pharmacopœias, all direct cold water; but the British Pharmacopœia, strange to say, recommends infusion for two hours and then boiling for fifteen minutes, followed by expression.

Extractum Glycyrrhizæ Purum (*Pure Extract of Glycyrrhiza*).—Commercial extract of licorice is prepared in a crude way with boiling water, the decoction being evaporated and then mixed with powdered licorice root, starch, and other substances to give it the necessary firm consistence. It occurs both in the form of mass and rolls or sticks, and also in powder, but is not suited for liquid preparations on account of the large amount of insoluble matter present; hence the Pharmacopœia directs the preparation of a completely soluble extract, officially designated as pure extract of glycyrrhiza. The sweet principle of licorice root, glycyrrhizin, being present in the drug partly in an insoluble form, ammonia water is added to the water to insure its complete extraction as ammonium glycyrrhizate; after the alkaline menstruum has all been used, percolation is continued with chloroform water to prevent fermentative changes in the marc.

Extractum Hæmatoxyli (*Extract of Hematoxylon*, also known as *Extract of Logwood*).—The medicinal value of logwood lies in its astringent principle, which cannot be entirely extracted with cold water; hence boiling is directed by the *National Formulary*. It is important that all contact with metal be avoided on account of the tannin. The extract should yield a clear, purplish-red solution with water. Extract of hematoxylon is well adapted for the dry condition, as it is non-hygroscopic; its taste is sweetish and afterward astringent. The commercial extracts of logwood sold in boxes are not suitable for medicinal purposes, being only partly soluble in cold water.

Extractum Hydrastis (*Extract of Hydrastis*, also known as *Extract of Golden Seal*).—As in the case of extract of aconite, ½ per cent. of tartaric acid is added to the alcoholic menstruum to facilitate extraction of the alkaloid. After concentration of the percolate to a soft extract, magnesium oxide and starch are added, and the mixture dried, powdered, and weighed. Having assayed a portion of the powdered extract, sufficient dried starch is finally added so that the finished product shall contain 10 per cent. of the ether-soluble alkaloid.

The Pharmacopœia requires that powdered extract of hydrastis, when assayed gravimetrically, shall yield not less than 9 per cent. nor more than 11 per cent. of the ether-soluble alkaloids of the drug.

Extractum Hyoscyami (*Extract of Hyoscyamus*).—As henbane is very variable in its alkaloidal content and the same menstruum is directed by the Pharmacopœia for the pilular extract as for the fluid-

extract, a carefully standardized fluidextract may be conveniently used for the preparations of this extract, which should contain 0.25 per cent. of the total alkaloids of the drug.

The Pharmacopœia requires that extract of hyoscyamus, when assayed by titration with tenth-normal sulphuric acid, shall yield not less than 0.215 per cent., nor more than 0.288 per cent. of the total alkaloids of hyoscyamus.

Extractum Ignatiæ (*Extract of Ignatia*).—Although the *National Formulary* directs that this extract shall be in dry powder form, no provision is made for removal of the fatty matter present in the bean, which surely will be extracted by percolation with alcohol. It would seem desirable to remove the fat in the manner directed in the case of extract of nux vomica, so as to insure the possibility of perfect pulverization. Having weighed the dry extract and assayed a portion of the same, sufficient dried starch is added, so that the finished product shall contain 6 per cent. of the total alkaloids of ignatia bean.

Extractum Jalapæ (*Extract of Jalap*).—This extract contains all the active resinous principles of the crude drug and differs from the official resin of jalap mainly in being of pilular consistence, and in containing some water-soluble constituents which are removed in the case of the resin.

Extractum Krameriæ (*Extract of Krameria*, also known as *Extract of Rhatany*).—Cold water is an excellent solvent for the particular tannin present in rhatany, upon which the astringency of the drug depends. The *National Formulary* directs that the dry powdered extract, obtained by evaporation of the aqueous percolate, be mixed with sufficient dried starch so that the finished product shall represent four times its weight of the crude drug. Krameria yields about 12 to 15 per cent. of dry extract when treated with cold water.

Extractum Leptandræ (*Extract of Leptandra*).—Leptandra yields about 12 per cent. of dry extract, consisting chiefly of resinous matter, when exhausted with the menstruum directed by the *National Formulary*, alcohol 3 volumes and water 1 volume. The dry extract having been powdered and weighed, sufficient dried starch is added so that the finished product shall represent four times its weight of the crude drug.

Extractum Malti (*Extract of Malt*).—Since diastase, the chief active constituent of malt, is destroyed by a temperature approaching that of boiling water, it is essential that the temperature prescribed in the official process of manufacture be not exceeded. Evaporation of the infusion at a low temperature in a vacuum apparatus is always to be preferred, the average yield being about 60 to 65 per cent. of extract. Extract of malt is a brownish-yellow, thick liquid or semifluid mass, having a slight peculiar odor, a sweet taste, and an acid reaction toward litmus paper.

The diastasic value of extract of malt is determined by its power of converting starch into dextrose, and the following method may be employed for comparative testing of different malt extracts, that

extract capable of converting the largest amount of starch within a given time, under like conditions, being considered the best: Dissolve 5 Gms. of extract of malt in sufficient distilled water to yield 100 mils. (or Cc.) of solution; of this, add 5 mils. (or Cc.) representing 0.25 Gm. of the extract, to 250 mils. (or Cc.) of cold starch mucilage (prepared by dissolving 30 Gms. of Bermuda arrowroot in 1000 mils. (or Cc.) of boiling distilled water) and keep the mixture at a temperature of 55° to 60° C. (131° to 140° F.) for thirty minutes; then stop the diastasic action by raising the temperature to 100° C. (212° F.) or by addition of 2 or 3 mils. (or Cc.) of a 10 per cent. sodium hydroxide solution, and dilute the mixture to a given volume by addition of water. Titrate an aliquot part of the liquid with Fehling's Solution (alkaline cupric tartrate volumetric solution, U. S. P.) and ascertain the amount of dextrose present, from which deduct the amount found in a corresponding amount of the extract of malt by previous titration with Fehling's Solution; the difference indicates the amount of sugar produced by the diastase present in the extract. Each mil. (or Cc.) of Fehling's Solution corresponds to 0.005 Gm. of anhydrous dextrose, or 0.0045 Gm. of starch converted thereinto.

Extractum Nucis Vomicæ (*Extract of Nux Vomica*).—The official directions for the preparation of this extract provide for the removal of the fatty matter taken up by the menstruum, by treating the concentrated percolate with two successive portions of purified petroleum benzin. As the fat also carries with it some of the alkaloidal constituents of the drug, the mixed benzin solutions are treated in a separator with very dilute sulphuric acid; the acid washings having been made alkaline with ammonia water are extracted with chloroform, and the chloroform solution of alkaloids is then added to the residue left after the second treatment with the benzin. The mixture is evaporated to dryness, powdered, weighed and assayed, and finally sufficient of a mixture of magnesium oxide 1 part and dried starch 3 parts is added, so that the finished product shall contain 16 per cent. of total alkaloids. The necessary amount of diluent may be ascertained by calculation, as shown in the case of powdered extract of aconite (see p. 345).

The Pharmacopœia requires that the powdered extract of nux vomica, when assayed by titration with tenth-normal sulphuric acid, shall yield not less than 15.2 per cent., nor more than 16.8 per cent. of the total alkaloids of the crude drug.

Extractum Opii (*Extract of Opium*).—This extract can be made from either moist opium or powdered opium; in the former case, the official directions for exhausting the drug will yield good results, but for the pharmacist, who may desire to make a smaller quantity of the extract, the use of powdered opium will prove less troublesome. As opium is easily exhausted with cold water, the powdered drug may be shaken to a smooth paste with water in a flask, more water then added and the whole frequently and vigorously shaken during twelve hours; the

mixture is then poured into a plain filter, allowed to drain and percolated with cold water until the opium is exhausted, as shown by the absence of color and only a faintly bitter taste in the percolate. The liquid is evaporated to dryness, powdered, weighed and assayed, sufficient dried starch being finally added, so that the finished product shall contain 20 per cent. of anhydrous morphine.

The necessary amount of dried starch to be added for adjustment of the morphine strength may be ascertained by calculation, as shown in the case of extract of aconite (see p. 345).

The Pharmacopœia requires that powdered extract of opium, when assayed gravimetrically, shall yield not less than 19.5 per cent., nor more than 20.5 per cent. of anhydrous morphine. Such an extract represents about twice its weight of official moist opium.

Extractum Physostigmatis (*Extract of Physostigma,* also known as *Extract of Calabar Bean*).—This extract is made exactly like powdered extract of aconite, with a menstruum consisting of alcohol holding about ½ per cent. of tartatic acid in solution, the fatty matter being removed by treatment of the concentrated percolate with two successive portions of purified petroleum benzin. Dried starch is used as the diluent, and the finished product contains 1.95 per cent. of the ether-soluble alkaloids of the crude drug; the necessary amount of diluent to be added can be ascertained by calculation, as explained under extract of aconite (p. 345).

The Pharmacopœia requires that powdered extract of physostigma, when assayed by titration with tenth-normal sulphuric acid, shall yield not less than 1.7 per cent. nor more than 2.3 per cent. of the alkaloids of physostigma.

Extractum Podophylli (*Extract of Podophyllum*).—The *National Formulary* directs a menstruum of alcohol 4 volumes and water 1 volume, the percolate to be evaporated to a pilular consistence. This extract would seem well adapted for the powdered form, as the activity of podophyllum resides in the resinous matter present, and could then be made with alcohol alone, as is the official fluidextract, and be standardized to represent a definite weight of the crude drug.

Extractum Quassiæ (*Extract of Quassia*).—Owing to the tendency of this extract, if in pilular condition, to become tough in the course of time, it seems preferable to have it in the powder form; and since the yield of extract obtained by exhausting quassia with cold water is small, rarely above 4 per cent., the *National Formulary* directs dilution with sufficient dried starch so that the finished product shall represent ten times its weight of the crude drug. In this condition the extract is well adapted for all purposes, is perfectly soluble in water, and keeps well.

Extractum Rhei (*Extract of Rhubarb*).—Since the menstruum directed for the preparation of extract of rhubarb is identical with that ordered for the fluidextract, small quantities of the extract can be conveniently made by evaporation of the latter to dryness and in-

corporation of calcined magnesia (5 Gms. for every 100 mils. (or Cc.) of fluidextract evaporated) and sufficient dried starch to bring the weight of finished product to one-half of that of the crude drug represented by the fluidextract. The weight of dry residue from the fluidextract varies from 35 to 42 Gms. for every 100 mils. (or Cc.). The powdered extract keeps well.

Extractum Stramonii (*Extract of Stramonium*).—Both the pilular and the powdered extract of stramonium are made exactly like the corresponding extracts of belladonna leaves, but contain less alkaloid, the official requirement being 1 per cent. The pilular extract is chiefly used in the preparation of ointments, and has a rich green color.

The Pharmacopœia requires that both the pilular and powdered extract, when assayed by titration with tenth-normal sulphuric acid, shall yield not less than 0.9 per cent., nor more than 1.1 per cent. of the alkaloids of stramonium.

Extractum Sumbul (*Extract of Sumbul*).—This extract can be conveniently made by evaporation of the official fluidextract, since the same menstruum is directed for both preparations. The Pharmacopœia directs that extract of sumbul shall be of pilular consistence, but this condition is difficult to obtain, owing to the peculiar nature of the resin and oil present in sumbul root. The yield of extract is about 15 per cent.

Extractum Taraxaci (*Extract of Taraxacum*, also known as *Extract of Dandelion*).—Although this extract was at one time directed to be prepared by expression and evaporation of the juice of the root freshly gathered, it is doubtful whether this plan was followed to any great extent, and, moreover, no provision was made for the removal of the starchy and albuminous constituents of the juice. The exhaustion of the ground taraxacum with a weak alcoholic (about 12 per cent.) menstruum insures complete extraction of the medicinal virtues, without much inert matter, the resulting pilular extract yielding a nearly clear solution with water. Absence of a bitter taste in the last portions of the percolate indicates complete exhaustion of the drug.

Extractum Viburni Prunifolii (*Extract of Viburnum Prunifolium*, also known as *Extract of Black Haw*).—Diluted alcohol appears to extract all the valuable constituents of the bark; after reduction of the percolate to a soft extract calcined magnesia is added, the mixture dried by exposure to currents of warm air, then powdered and weighed, and sufficient dried starch finally added, so that the finished product shall represent five times its weight of the crude drug from which it is made.

CHAPTER XXIV.

OLEORESINS AND RESINS.

OLEORESINS.

SOLUTIONS of this class represent the medicinal virtues of the drugs from which they are made, in a more concentrated form than is possible in any other. They possess the power of self-preservation, and in this respect are superior to fluidextracts. Oleoresins consist chiefly of fixed or volatile oils associated with resin and other constitutents; those officially recognized, with one exception, are all prepared by the same process, which consists in slowly percolating the drug in fine powder, with ether, to exhaustion, recovering the greater part of the ether by distillation, and finally removing the remaining ether by spontaneous evaporation. The percolation of drugs with ether requires the use of special apparatus (see page 147) to prevent loss of the volatile solvent, and several attempts have been made to economize menstruum by repeatedly using the same liquid until the material is exhausted, the best device for this purpose being the ether extraction apparatus designed by Prof. Flückiger, illustrated in Fig. 229. The extractor *A* passes by means of the tube *D* through a cork into the receiving flask *E;* at *C* is a septum or disk, upon which the material to be extracted is packed, and which communicates by means of a small funnel-shaped tube with *D*. The lateral tube *BF* passes into the tube *G*, which is provided with a properly cut cork, *K*, so that the ether vapor may pass from the receiving bottle to a spiral condenser, *H*, fitted by means of a cork to the top of the extractor; the ether vapor can also be made to pass upward through the powder by pushing the cork deeper into the tube *G*, thus closing the orifice of the lateral tube *BF*. A loose pledget of cotton is placed in the funnel tube at *C*, or a piece of filter paper is placed over the small opening to prevent the material from passing down. The whole apparatus may be made of any convenient size, of glass or tinned copper, and when in use the receiving flask is placed in warm water, for the purpose of vaporizing the ether, which is condensed above the extractor and drops back upon the powder, the process being continued until the material is exhausted. Another desirable feature of this apparatus is the recovery of the ether from the marc when the extraction of the drug has been completed. The lateral communication between *D* and *BF* is closed by means of the cork, and, applying a cold wet sponge to the receiving flask, the ether vapor therein is condensed and a partial vacuum produced which withdraws all the ether from the marc in the percolator above.

Experience has shown that when 2 mils. (or Cc.) of percolate have been obtained for each Gm. of drug used, the latter will be practically exhausted, therefore percolation beyond this point is unnecessary; with the continuous extraction apparatus, half the quantity of ether can be made to accomplish the same results.

Some care is necessary in the recovery of ether by distillation, as official ether, which is directed to be used in the process, boils at about 35° C. (95° F.); the recovered ether should be but very slightly impregnated with the odor of volatile oil, and may be used for a subsequent operation. Oleoresins are not used to any great extent at present, and are rarely made by the pharmacist himself; small quantities for use in prescriptions may be conveniently obtained by percolating some of the finely powdered drug in the barrel of a glass syringe and allowing the ether to evaporate in a warm place. The yield of oleoresins ranges from 5 to 60 per cent. for different drugs, and their consistence varies from liquid to a soft solid, dependent upon the amount of resin present.

On account of the very volatile nature of ether, which makes percolation with this menstruum unsatisfactory in summer, when the temperature at times rises above the boiling point of ether, acetone was suggested by Beringer as early as 1892 for the preparation of oleoresins, and was officially directed in the last Pharmacopœia. The results obtained with acetone, which has a boiling point of about 56.5° C. (133.7° F.) or about 20° above that of ether, have proven very satisfactory. Oleoresins prepared with acetone are perfectly soluble in ether, and drugs exhausted with acetone, when subsequently percolated with ether, have been found to yield nothing of value to the latter solvent.

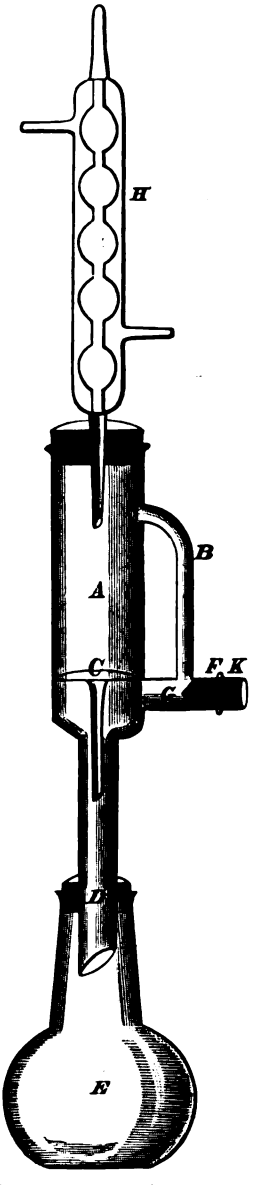


FIG. 229.—Flückiger's ether-extraction apparatus.

The Pharmacopœia recognizes 5 oleoresins prepared with ether and 1 with alcohol, and in every case the drug is packed firmly into the percolator, previous moistening being unnecessary. The following is an alphabetical list of the official oleoresins, showing the fineness of powder used and the average yield:

LIST OF OFFICIAL OLEORESINS.

Latin name.	English name.	Fineness of Powder.	Average Yield.
Oleoresina Aspidii	Oleoresin of Aspidium	No. 60	15 per cent.
Oleoresina Capsici	Oleoresin of Capsicum	" 60	12 " "
Oleoresina Cubebæ	Oleoresin of Cubeb	" 30	22 " "
Oleoresina Petroselini	Oleoresin of Parsley Fruit	" 60	21 " "
Oleoresina Piperis	Oleoresin of Pepper	" 60	6.5 " "
Oleoresina Zingiberis	Oleoresin of Ginger	" 60	6 " "

SPECIAL REMARKS.

Oleoresin of Aspidium, also known as *Oleoresin of Male Fern.*—This preparation is known also by the names *oleoresina filicis, extractum filicis æthereum,* and *oleum filicis maris.* As the root rapidly deteriorates upon keeping, only that having a fresh green color should be used. The oleoresin of male fern generally deposits, on standing, a granular crystalline substance largely composed of filicic acid, upon which depends the activity of the preparation; hence the necessity for thoroughly incorporating the deposit before dispensing the oleoresin. By percolation with acetone the drug has yielded as much as 18 per cent. of oleoresin. This preparation is recognized in the British Pharmacopœia as Extractum Filicis Liquidum, and in the German Pharmacopœia as Extractum Filicis.

Oleoresin of Capsicum.—Owing to the large amount of fat present in capsicum it is not desirable to carry percolation to complete exhaustion; experience, in fact, has taught that, if collected slowly, 150 mils. (or Cc.) of percolate will have practically exhausted 100 Gms. of the drug, and that further treatment simply loads the percolate with fatty matter. Oleoresin of capsicum is a dark, brownish-red liquid, which, shortly after being made, deposits granular fat; this is best removed be decanting the clear liquid and straining the residue or washing the deposit with a little ether. Although the average yield of oleoresin has been reported as not over 5 or 6 per cent., from 12 to 16 per cent. of a very excellent preparation has very frequently been obtained.

Oleoresin of Cubeb.—Cubeb yields all its medicinal virtues to alcohol as well as ether; very satisfactory oleoresin has been made with alcohol alone, and this menstruum is now used by many manufacturers. In Germany the oleroresin is officially recognized under the name *Extractum Cubebarum,* and is prepared with a mixture of equal volumes of ether and alcohol. All oleoresin of cubeb deposits, upon standing, waxy matter and a crystalline body, cubebin, which, as the Pharmacopœia directs, should be rejected, only the liquid portion being dispensed. It is of a green or brownish-green color, and when made with ether has been obtained to the extent of 25 per cent.

Oleoresin of Ginger.—When made from uncoated (Jamaica) ginger the yield of oleoresin is less than from coated ginger, and is also lighter in color, thinner, and of a more agreeable flavor. The name *piperoid* has sometimes been applied to this preparation. From coated ginger as much as 10 per cent. of oleoresin has been obtained, while from Jamaica ginger the yield rarely exceeds 6 per cent.

Oleoresin of Parsley Fruit.—This oleoresin, also called liquid apiol, occurs as a dark green liquid of about the same specific gravity as water. Upon standing it sometimes deposits waxy matter and hence the Pharmacopœia directs that it shall be set aside for four or five days and then decanted from any solid matter that may have separated. The average yield is about 21 per cent.

It is unfortunate that the name liquid apiol is commonly applied to oleoresin of parsley fruit, and it should not be confounded with apiol or parsley camphor. The latter is official in the French Pharmacopœia and is given the formula $C_{12}H_{14}O_4$. It is also known as *apiol blanc* or white apiol and occurs in large needle-shaped crystals, which melt at 30° C. (86° F.), and may be obtained by refrigeration of the volatile oil of parsley seed. Apiol is insoluble in water, but soluble in alcohol and ether.

Oleoresin of Pepper.—Commercially this preparation is known also as *oil of black pepper*, which latter, however, is usually obtained as a by-product in the manufacture of piperin. Oleoresin of pepper, when first made, deposits piperin in crystalline form, which is separated by straining, leaving a thick, very black liquid. The yield with ether or acetone rarely exceeds 6.5 per cent.

RESINS.

Under the title *Resinæ* the Pharmacopœia recognizes 4 preparations, 1 of which, however, is simply a residuary product obtained in the distillation of the volatile oil from a natural oleoresin. For the remaining 3 an official process of manufacture is given, alcohol being used as a solvent in each case; the resin is obtained by pouring a concentrated alcoholic tincture of the respective drugs into cold water and subsequently washing the precipitate repeatedly with water.

ALPHABETICAL LIST OF THE OFFICIAL RESINS.

Latin name.	English name.	Mode of obtaining.
Resina	Rosin	Residue left after distillation of the volatile oil from Turpentine.
Resina Jalapæ	Resin of Jalap	By pouring a concentrated alcoholic tincture of jalap into cold water, washing the resulting precipitate twice with fresh portions of hot water, and, after draining off all liquid, heating the resin on a waterbath to dryness.
Resina Podophylli	Resin of Podophyllum	By pouring a concentrated alcoholic tincture of podophyllum into cold water acidulated with hydrochloric acid.
Resina Scammoniæ	Resin of Scammony	By pouring a concentrated alcoholic tincture of scammony root into hot water, washing the precipitated resin twice with hot water, and drying.

SPECIAL REMARKS.

Resin of Jalap.—The amount of resin in jalap root varies considerably, ranging from 6 to 18 per cent., and it is not always possible to find commercial jalap, which exceeds the official requirement of *not less than 7 per cent.* of resin, although prime lots yielding from 12 to 15 per cent. are occasionally met with. Resin of jalap is soluble in alcohol in all proportions, the solution having a slight acid reaction to litmus paper; it is also soluble slowly in five times its weight of 10 per cent. ammonia water, but is insoluble in fixed and volatile oils. The Pharmacopœia requires that not more than 12 per cent. of the resin shall be soluble in ether, and not more than 30 per cent. in chloroform; also that its solution in five times its weight of ammonia water shall not become gelatinous on standing, and when acidulated with hydrochloric acid only a slight turbidity shall appear, showing the absence of rosin, guaiac, and other resins. The presence of common rosin may also be detected by solubility in oil of turpentine and by acquiring a pink color if 0.02 Gm. of resin of jalap be dissolved in 2 mils. (or Cc.) of glacial acetic acid and a few drops of sulphuric acid then added. Since resin of jalap has a slightly acrid but not bitter taste, an adulteration with aloes may be suspected if a pronounced bitter taste is observed. If resin of jalap be moistened with alcohol and then with a solution of ferric chloride, a green color should not be developed, nor should a blue color be observed if the inner surface of a fresh potato paring be rubbed with the resin, otherwise guaiac is present. The limit of acid resins is determined by adding 0.5 mil. (or Cc.) of half-normal alcoholic potassium hydroxide solution to a solution of 1 Gm. of resin of jalap in 50 mils. (or Cc.) of alcohol containing 1 mil. (or Cc.) of phenolphthalein test-solution, when a red color should be produced.

Resin of jalap may be obtained free from color by treatment with animal charcoal; the best plan is to mix the charcoal with the powdered jalap before percolation, and also to pass the percolate through animal charcoal.

Resin of Podophyllum.—The object of adding hydrochloric acid to the water before adding the alcoholic solution is simply to facilitate the separation of the resinous matter. The yield of resin of podophyllum rarely exceeds 4 or 5 per cent., and its color may vary from light brown to greenish-yellow, turning darker when subjected to a temperature exceeding 25° C. (77° F.). According to Prof. Lloyd, who has had large experience in the manufacture of this resin, the concentration of the alcoholic tincture should not be carried beyond a very thin syrup, the water into which it is poured should be ice-cold, and the washed resin should be dried *without* heat, by exposure to air in a cold place. Alum water is sometimes used to effect precipitation of the resin, but it yields a yellow product of inferior quality. The Pharmacopœia requires that resin of podo-

phyllum shall dissolve in alcohol with only a slight opalescence, and that not less than 75 per cent. of the resin shall be soluble in ether and not less than 65 per cent. in chloroform; also that it shall not yield more than 1.5 per cent. of ash. The solubility of resin of podophyllum in ether varies from 50 to 85 per cent., depending upon the mode of its preparation, the better quality being most soluble and also lighter in color; according to F. B. Power, boiling water will dissolve about 80 per cent. of the resin if the treatment with fresh portions of the water be continued as long as anything is removed, but deposits most of it again on cooling. Resin of podophyllum is intensely irritating to the mucous membranes, especially of the eye, and care should be exercised in handling it. It forms a deep yellow liquid with solution of sodium or potassium hydroxide, from which it is reprecipitated by acids.

The official resin of podophyllum may be distinguished from the resin obtained from Podophyllum Emodi, by adding 0.5 mil. (or Cc.) of potassium hydroxide test-solution to a mixture of 0.4 Gm. of the resin and 3 mils. (or Cc.) of 60 per cent. alcohol and gently shaking; the mixture should not gelatinize.

Resin of Scammony.—The Pharmacopœia directs that this resin be prepared by pouring a concentrated alcoholic tincture of scammony root, in form of a syrup, slowly and with constant stirring into hot water. After decantation of the supernatant liquid, the precipitated resin is washed twice with fresh portions of hot water and then dried on a waterbath. Resin of scammony should dissolve in alcohol in all proportions, and not less than 95 per cent. of it should dissolve in ether, which distinguishes it from resin of jalap and resin of false scammony. It differs from the gum-resin of scammony in not forming an emulsion with water.

Resin of scammony is soluble in ammonia water and in solutions of the fixed alkalies with the aid of a gentle heat, and such solutions, like those of resin of jalap, are not precipitated by addition of dilute acids; its almost complete solubility in ether will serve to detect the presence of jalap resin. An adulteration with rosin can be detected by stirring resin of scammony with an equal weight of sulphuric acid, when the latter should not turn red; if guaiac has been added, an alcoholic solution of the resin will give a blue color on addition of hydrogen dioxide solution or ferric chloride test-solution. The Pharmacopœia requires that upon incineration resin of scammony shall not yield more than 1 per cent. of ash.

CHAPTER XXV.

COLLODIONS.

UNDER this head are recognized in the Pharmacopœia and *National Formulary* 8 solutions, the base of which is pyroxylin, or soluble guncotton (see Cellulose, Part III), and the solvent, a mixture of alcohol and ether. Collodions are employed only for external medication, and owing to the very volatile character of the solvent they rapidly form a skin-like covering, or pellicle, when applied, which is impervious to water. Where a strong contractile coating is desired, the plain collodion is preferred, otehrwise a less constringent and more comfortable covering is obtained by the addition of castor oil as in the case of the official flexible collodion. For the purpose of medication, any substance soluble in ether may be added, such as iodine, iodoform, extract of Indian cannabis, salicylic acid, croton oil, mercuric chloride, veratrine, atropine, resorcin, pyrogallol, etc. Since pyroxylin is insoluble in water, the addition of the latter to collodion would cause immediate precipitation, hence all substances soluble only in water or alcohol and water, such as extract of belladonna, morphine sulphate, etc., are excluded from admixture. Collodions should always be preserved in tightly cork-stoppered bottles, in a cool place, remote from fire, on account of the ether present; care should also be taken that no collodion be allowed to remain on the lip or in the neck of the bottle after pouring out the liquid, to avoid "fixing" of the cork as the menstruum evaporates.

Collodions are best dispensed in small round-shouldered vials provided with a cork through which a camel-hair pencil has been passed and securely fastened; this avoids loss of material and drying of the collodion in the brush—a very annoying occurrence.

ALPHABETICAL LIST OF U. S. P. AND N. F. COLLODIONS.

Latin name.	English name.	Method of preparation.
Collodium . . . U. S. P.	Collodion . .	Made by dissolving pyroxylin in a mixture of alcohol and ether, and after the liquid has become clear, decanting the latter from any sediment formed.
Collodium Cantharidatum . . . . . U. S. P.	Cantharidal Collodion . . .	Made by dissolving an acetous acetone extract of cantharides in flexible collodion. The finished product represents 60 per cent. of cantharides.
Collodium Flexile . U. S. P.	Flexible Collodion	Made by mixing 3 parts of castor oil 2 parts of camphor, and 95 parts of collodion, all by weight.

Latin name.	English name.	Method of preparation.
Collodium Iodi Nat. Form.	Iodine Collodion	Made by dissolving iodine in flexible collodion. It is a 5 per cent. solution.
Collodium Iodoformi Nat. Form.	Iodoform Collodion	Made by dissolving iodoform in flexible collodion. It is a 5 per cent. solution.
Collodium Salicylici Compositum Nat. Form.	Compound Salicylic Collodion	Made by adding fluidextract of Indian cannabis to a solution of salicylic acid in flexible collodion. The name Corn Collodion is frequently applied to this preparation.
Collodium Stypticum Nat. Form.	Styptic Collodion	Made by dissolving tannic acid in flexible collodion.
Collodium Tiglii Nat. Form.	Croton Oil Collodion	Made by dissolving croton oil in flexible collodion. It is a 10 per cent. solution.

SPECIAL REMARKS.

Collodion.—If the pyroxylin has been carefully prepared, it should be perfectly soluble in the official menstruum, although a slight sediment of dirt, etc., occurs after the solution has been set aside for a few hours; from this the liquid can be carefully poured off, as filtration is impracticable. Anthony's collodion cotton, specially prepared for photographers' use, has been found very satisfactory.

Cantharidal Collodion.—The value of cantharidal collodion will depend upon the quality of the powdered cantharides used and the care with which it has been exhausted. A mixture of glacial acetic acid and acetone is preferred as a menstruum since it has been found that the preparation, when made with a chloroform extract of cantharides, as formerly directed, is liable to gelatinize upon standing for some time. The extract dissolves readily in flexible collodion, by agitation, the finished product representing 60 per cent. of its weight of powdered cantharides, which makes it nearly twice as strong as the official cerate of cantharides.

Flexible Collodion.—The addition of camphor and castor oil imparts to collodion the property of forming a flexible pellicle which, while serving as an impervious covering to the part affected, yet permits of perfect freedom of motion.

CHAPTER XXVI.

EMULSIONS.

THE term "emulsion" is applied in pharmacy to a more or less permanent mixture of fixed oils, volatile oils, ether, chloroform, oleoresins, or resins with water, the former substances being suspended in a minutely divided state, resulting in an opaque milk-like liquid, varying from a thin-fluid to a thick-fluid condition according to circumstances. Types of such emulsions are found in nature in the case of milk and the milk-like juices of certain plants from which the official and other gum-resins are obtained.

In physics and physical chemistry the term is used in a less restricted sense, and of late years much work has been done with the view of arriving at a satisfactory explanation of the various conditions met with. The term internal phase has been applied to the substance emulsified or dispersed, while the vehicle or dispersion medium has been called the external phase. Solid as well as liquid emulsions can be obtained, as shown in the case of the official hydrous wool fat or lanolin, where a considerable quantity of water, divided into minute droplets, is dispersed in a fat solid at ordinary temperature, forming a permanent uniform mixture; another instance of a solid emulsion, in which water is dispersed in fat, is butter.

Theory of Emulsification.—The most plausible theory of the formation of emulsions is that an insoluble liquid or solid, in a state of minute division, is surrounded or enveloped by a thin film of the dispersion medium, which prevents the minute particles from aggregating or coalescing. Colloidal solutions (see p. 136) are undoubtedly closely allied to emulsions, and the term emulsion has also been applied to such intimate suspensions in magma form, as milk of magnesia.

Emulsions prepared by pharmacists may conveniently be divided into natural and artificial; to the former class belong those which are made from seed or gum-resins, by simple trituration with water, Nature having provided the necessary emulsifying agent in intimate association with the oil or resin. Artificial emulsions are such as require the addition of some foreign body, by means of which the suspension of the oil or resin is made possible; to this class belong the majority of the emulsions prepared at the dispensing counter. Fixed and volatile oils, as well as ether, chloroform, oleoresins, and resins, are suitable for exhibition in the form of emulsion, the suspension in water being accomplished by the aid of appropriate excipients, such as acacia, tragacanth, yolk of egg, casein, dextrin, Irish moss, gelatin, soap-bark, etc. Oil-yielding seeds and natural gum-

resins contain albuminous and mucilaginous matter, by means of which the oil and resin can be brought into perfect suspension in water by careful trituration.

Stability of emulsions, while primarily dependent upon division of the immiscible liquids into minute particles or globules, is materially influenced by the viscosity of the vehicle, whereby the surface tension of the liquids forming the emulsion is more nearly equalized, and the adhesion between the surfaces overcomes the inherent cohesive force of the separate particles. Solutions of acacia or of gelatin and mucilage of Irish moss or of tragacanth serve as such stabilizers and their power of preventing coalescence or separation of individual particles is no doubt due to their condition of hydrated colloids when in solution. Occasionally a combination of the above-named agents has been found advantageous, and the German Pharmacopœia directs the use of acacia, gelatin and tragacanth for its official emulsion of codliver oil with calcium hypophosphite. To prevent the fermentative changes likely to arise in all aqueous vegetable solutions, alcohol or glycerin is frequently added to emulsions, in the proportion of 1 or 2 fluidounces for every pint.

All emulsions, except those of volatile oils, chloroform or ether, should be made in a mortar, either of unglazed Wedgwood ware or porcelain, having a flat bottom, and, in the case of seed or gum-resin emulsions, one of deep shape provided with a hard wood pestle is to be preferred, in order to avoid injury from the force often necessary in crushing and manipulating the material. For making gum-resin emulsions, the cleanest and best tears should be selected, as the commercial fine powders are unfit for this purpose, partly because they are inferior in quality, and partly because they have been so modified by drying that when triturated with water they form simply an ordinary mixture from which the powder separates rapidly on standing; this change is due to dehydration, whereby the natural association of gum and resin has been broken up and their intimate union destroyed. For seed emulsions, when no other proportions are specified, 1 part of seed is used to 10 parts of water, all dirt and dust being carefully removed, if necessary, by washing with cold water. In both cases the material is crushed into a coarse powder, and, after the addition of a small quantity of water, beaten into a perfectly smooth, pasty mass; to this the remainder of the water is then added in divided portions, triturating the mass thoroughly and keeping it well scraped from the pestle and sides of the mortar, so that a uniform mixture may result, which is finally passed through a well-wetted strainer of loose flannel or cheesecloth, to remove the inert woody fiber and possible impurities. In making emulsion of lycopodium, it becomes necessary to triturate the seed *dry, with some pressure,* in order to rupture the hard seed envelope; when the powder changes in color and becomes damp and adhesive from the oil, a little water is added, with which a smooth, soft paste can be formed, to be further diluted by the addition of

water as directed above. Emulsion of lycopodium *should never be strained*, and, if properly made, will show no particles floating on the surface; the insoluble matter which settles upon standing is readily reincorporated by agitation.

Oil emulsions, which are far more frequently used (at least in this country) than those made from seed or gum-resins, require more care in their preparation, as success depends not only on the manipulation, but also on the judicious choice of an excipient. As a general rule it may be stated that acacia produces the whitest and most stable emulsions, because its perfect and ready solubility in water enables the operator to divide the oil quickly into minute globules, which are at once surrounded by an envelope of the mucilaginous liquid and thus kept from coalescing. The oil globules of a well made acacia emulsion, when compared with milk under a magnifying lens, more closely resembles its fat globules than would be the case if made with other excipients. To insure success, it is essential that definite proportions of oil, gum, and water be used for making the primary emulsion, which can then be diluted with water as desired. *Not less than one-fourth nor more than one-half* as much acacia as oil should be used, and *not less than one and a half times nor more than twice as much* water as acacia. The mixing of oil, gum and water should not be effected by the usual method of trituration, which involves pressure of the pestle against the material on the bottom and sides of the mortar, and consequent development of heat, but should be brought about by a rapid, light rotary movement of the wrist, communicated to the pestle held loosely in the hand, as shown in Fig. 230; this motion partakes more of that of an egg-whip, and the oil is thus rapidly broken up into minute globules in the presence of a viscid solution.

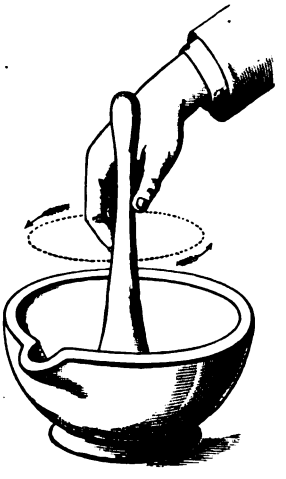


FIG. 230.

As stated before, emulsions of fats and fixed oils are best made in a flat-bottomed mortar, three distinct methods being in use to effect the desired object, namely, a milk-like liquid, miscible with water without the separation of oil globules. By many pharmacists the method usually recommended in Great Britain is preferred; this consists in making a smooth, thick mucilage of granulated acacia and water, and then adding the oil by degrees, stirring assiduously until each portion of oil is emulsified—lastly adding the water for dilution, in divided portions. The other two are sometimes called the "Continental" methods, from the fact that they are used almost exclusively in Continental Europe. They do not direct the previous solution of

the gum in water, and adhere strictly to definite proportions. While the so-called "English" method yields very satisfactory results in the hands of those accustomed to it, for the inexperienced either of the other two methods is to be much preferred, such preference being based upon observation of many hundred cases in the hands of students working in the laboratories in charge of the author, who has never known of a single failure by a novice to make a perfect emulsion according to the following methods, provided, of course, that the directions as given were followed.

Place in a mortar one-fourth as much *finely powdered* acacia as the oil to be used (7.5 Gms. of acacia for 30 mils. (or Cc.) of oil, or ℥ij for f℥j), then add the oil and triturate well together into a smooth mixture. Now add *all at once*, not gradually, twice as much water as the acacia which has been used (15 mils. (or Cc.) of water for 7.5 Gms. of acacia, or f℥iv for ℥ij), and stir rapidly until a perfect emulsion has been formed, which is known by the appearance of a white, pasty mass, free from oil particles, and a peculiar crackling noise as the pestle is drawn through the adhesive mixture. This primary emulsion should be well scraped with a spatula from the pestle and sides of the mortar, again stirred, and then the remainder of the water slowly added with constant stirring. Granulated acacia cannot be used in this method, as with so small a quantity of gum it is necessary that it dissolve almost immediately, which will not occur with the granulated variety.

The second of the so-called "Continental" methods directs increased proportions of acacia and water, by which means an equally perfect, and at the same time denser, primary emulsion is obtained. One-half as much granulated acacia as oil is used, and one and a half times as much water as gum, or one-half as much water as oil and gum together; thus, oil 30 mils. (or Cc.) or f℥j, granulated acacia 15 Gms. or ℥iv, and water 22.5 mils. (or Cc.) or f℥vj. Place the acacia in a dry mortar, add the oil and water, and stir briskly until a perfect emulsion results, which dilute with the remaining water, as in the preceding method.

If from any cause the primary emulsion should fail, it will prove a loss of time and labor to endeavor to save it by the addition of gum or water, provided the right proportions were used in the first place; the best plan is to begin over again and observe care in details. Assiduous stirring or shaking is of no avail in trying to save a "cracked" emulsion, which has a pearly appearance in the mortar, and the further addition of gum, while increasing the density of the mixture, does not always remedy the trouble.

The above methods are equally well adapted for liquid oleoresins, such as copaiba, oleoresin of cubeb, etc. If solid fats, camphor, some oleoresins and resinous extracts, as, for instance, extract of Indian cannabis, are to be administered in aqueous liquids, it will be found advantageous to dissolve them in a small quantity of fixed oil (oil of sweet almond or olive oil), and then to emulsify them in the manner

directed for these oils. Salol, menthol, thymol, phosphorus, and other substances can likewise conveniently be emulsified after solution in some fixed oil. The emulsification of Peru balsam, will be materially facilitated by the addition of a little oil of sweet almond, about 10 per cent. of the volume of balsam being, as a rule, sufficient. If emulsions of wax or spermaceti are to be made, heat must be employed; the wax or spermaceti is melted in a mortar heated to about 65° C. (149° F.) and mixed with an equal weight of powdered acacia, after which exactly one and a half times as much water as acacia, heated to near boiling, is added, and the mixture briskly stirred. After the emulsion cools to about 30° C. (86° F.) more water may be added in small quantities, with constant stirring. Whenever double emulsions are ordered, as, for instance, a seed emulsion with that of a fixed oil, better results will be obtained if separate emulsions be made and then mixed; when castor oil is to be mixed with emulsion of almond as a vehicle, the oil should be emulsionized with the requisite quantity of acacia and water, and this primary emulsion then diluted with the almond emulsion, out of which the water necessary for the previous emulsification of the oil has been retained.

Whenever an oil emulsion is made, the rule should be observed never to measure the water in an oily graduate, as otherwise oil particles might subsequently be carried into the mixture, and, failing to be emulsified, eventually rise to the surface. The view held by some authorities, that a good emulsion is capable of emulsifying additional quantities of oil, requires modification, as pointed out by Mr. Gerrard, of England; for, although a perfect fixed-oil emulsion admits of the incorporation of more oil, this latter oil will not undergo emulsification, but simply be mixed intimately, as can be proved by the addition of water, when the newly added oil will separate. A perfect artificial emulsion should have a milk-like appearance and consistence, be miscible with water without separation, should flow readily from the mortar without leaving any adhering particles, so that it can be washed with plain water, and, if separation takes place after standing at rest for some time, a cream-like layer should rise to the surface, which can be quickly reincorporated by agitation. Heat is detrimental to the permanence of emulsions and causes separation, so also large quantities of alcohol or saline matter. Substances which have a tendency to absorb water, such as magnesia, must not be mixed with the emulsion, unless previously completely hydrated. All salts should be added in the form of solution, and, together with tinctures and other alcoholic liquids, not until the primary emulsion has been properly diluted.

Emulsions of ether, chloroform, oil of turpentine, and other volatile liquids are best prepared by agitation in a bottle after the manner first suggested by Forbes. The liquid to be emulsionized is poured into a *perfectly dry* bottle and the powdered acacia added, after which the bottle is well shaken so that the acacia may become saturated

with the volatile liquid; water is then added and agitation continued until a homogeneous emulsion results, which can further be diluted by the gradual addition of water. Volatile oils and ethereal liquids will never form as perfect an emulsion as fixed oils, and separation of the mixture takes place more speedily; if care has been observed, however, in making the mixture, only a dense, creamy layer will rise to the surface, which can be reincorporated by agitation. As a rule volatile oils and ethers require more gum than fixed oils, and less than 30 grains of powdered acacia should not be used for each fluidrachm; the amount of water first added should always be equal to twice the acacia used. Oil of turpentine unites very readily with water and gum, and it is surprising to see how small a quantity of gum will suffice to form a perfect emulsion from which no oil will separate in an uncombined form, only a dense, creamy layer rising, composed of the oil of turpentine, gum, and some water in intimate union; 20 grains of powdered acacia shaken in a bottle with 1 fluidounce of oil of turpentine, and 4 fluidrachms of water then added, will yield a very satisfactory emulsion, which can be kept for days without separating an oily layer. All emulsions of volatile oils are more permanent if made with the aid of some fixed oil previously added to the volatile oil; such emulsions are preferably made in a mortar.

When powdered tragacanth is preferred as an emulsifying agent, it may be used in the proportion of one-tenth or one-eighth of the necessary weight of acacia, and requires from 10 to 20 times its weight of water; it should be thoroughly mixed with the oil in the mortar or bottle, as the case may be, and after the addition of water the mixture should be stirred rapidly or shaken until the primary emulsion has been formed. The division of oil globules by means of mucilage of tragacanth is much coarser than with acacia, hence tragacanth emulsions are never so white nor seemingly so perfect; but owing to the viscosity and magma-like condition of mucilage of tragacanth the oil globules, although not finely divided, are kept from reuniting, and thus separation of an oily layer is prevented. Mixtures of tragacanth and acacia are often employed, particularly in the emulsification of codliver oil, to obtain greater protection against separation.

Yolk of egg has long been known as a valuable excipient in emulsions, particularly when acids or large proportions of alcoholic liquids are to be added. One yolk from an egg of average size will suffice for 1 fluidounce of a fixed oil or for 1 fluidounce of a volatile oil; in place of the simple yolk, a solution of yolk of egg 45 parts, and glycerin 55 parts, known as glyconin, may be used with advantage, 2½ fluidrachms being required for ½ fluidounce of fixed oil. In either case the oil should be added in small quantities to the yolk of egg or glyconin, previously rubbed smooth in a mortar, each portion being thoroughly incorporated before another addition is made; if the mixture should become inconveniently thick, a small quantity of water may be introduced, and after all the oil has been emulsified the prescribed amount of

water is added, likewise in divided portions, with constant stirring. The readiness with which yolk of egg unites with fixed oils is due to the fact that it is itself a natural emulsion of an oil and albuminous matter. Some little care is necessary in removing the yolk of egg from the shell, to avoid contamination with the white or albumen, which has a tendency to form clots in the emulsions.

Of other emulsifying agents introduced during the last thirty years, none has been more extensively used, particularly on a large scale by manufacturers, than mucilage of Irish moss. Toward fixed oils the mucilaginous matter of Irish moss behaves somewhat like tragacanth, particularly if the solution of the former be made somewhat thick. This mucilage is made by washing the drug with cold water to remove saline and other foreign matter, then heating it with the required quantity of water in a dish, for fifteen minutes, on a boiling waterbath, and finally straining the mixture; the strength of the mucilage may be from 10 to 15 grains to the ounce, the usual strength being about 12 grains. Of the latter mucilage, 5 fluidrachms are considered sufficient for 1 fluidounce of oil, the emulsion being made by adding the oil in small portions to the mucilage contained in a bottle and agitating briskly after each addition; after all the oil has been emulsified, syrup or more water may be added as a diluent. Emulsions made with Irish moss are not so white as those made with acacia, and contain the oil in a coarser state of division; some manufacturers add acacia to the Irish moss mucilage, in order to improve the emulsion.

While milk itself is a very poor emulsifier of fats and fixed oils, its albuminoid constituent, casein, is said to be even superior to acacia. According to Leger, a French pharmacist, it is best used in the form of a saccharated powder, prepared as follows: To 4 quarts of milk warmed to 40° C. (104° F.) add 2½ fluidounces of ammonia water, and after setting aside for twenty-four hours withdraw the lower milk serum from the upper fatty layer. Precipitate the casein from the milk serum by the addition of acetic acid, and wash the precipitate by decantation with water warmed to about 40° C. (104° F.); finally collect on a wetted muslin strainer and express the moisture. Determine the amount of dry casein in the residue by heating a weighed portion to complete dryness in an air bath; add 10 Gms. of sodium bicarbonate and sufficient sugar to obtain, when dry, a powder containing 10 per cent. of its weight of casein. The mass must be dried at a gentle heat and powdered; it keeps well for a long time in securely corked bottles. For oil emulsions, Leger recommends the making of a mucilage of 15 parts of saccharated casein with 5 parts of water, and adding to this in small portions 15 parts of oil, stirring well after each addition; finally diluting the emulsion as required.

Condensed milk has also been successfully used as an emulsifying agent for castor oil and codliver oil. A fluidounce of the oil is mixed by trituration in a mortar, in small quantities, with ½ fluidounce of condensed milk, and, when emulsified, ½ fluidounce of water is slowly

added, with constant stirring. Such emulsions, however, do not bear dilution well.

Mucilage of dextrin, made by heating 1 ounce of white dextrin with 2 ounces of water until dissolved, has been recommended as an emulsifying agent, each fluidounce of fixed oil requiring 6 fluidrachms of the mucilage, which must be cooled just short of gelatinizing, but the results are not satisfactory.

Although soap is known to be an excellent emulsifying agent, its use is naturally confined to the preparation of liniments and other external remedies. Soft soap is even superior to hard soap and its efficiency is demonstrated in the official compound solution of cresol, forming an emulsion from which the cresol does not separate, and which is readily miscible with water. A solution of soap possesses far less viscosity than mucilage of acacia and similar liquids and yet its power of forming stable emulsions is greater in many instances; this is explained by considering soap as a colloid which forms with water a hydrate possessing remarkable dispersing properties and capable of emulsifying large quantities of oil, as shown in the case of the official ammonia liniment and lime liniment. The readiness with which olive oil and oil of turpentine can be dispersed in even a weak solution of soap, for use as enemas, is well known to physicians and nurses.

The saponaceous principles of quillaja and other drugs rich in saponins possess the property of dividing and suspending oil globules quite well if used in sufficient quantity. While the fluidextract and tincture of quillaja could be employed for this purpose, the toxic properties of the constituents render them undesirable and they should never be used without the knowledge and consent of the physician.

The *National Formulary* gives directions for preparing typical emulsions of codliver oil with different emulsifying agents, which are also applicable to other fixed oils and to liquid oleoresins. For flavoring emulsions a series of flavors is given, such as methyl salicylate, mixtures of methyl salicylate and oil of sassafras, methyl salicylate and oil of bitter almond, etc., of which from 1.5 to 5 mils. (or Cc.) may be used for 1 liter of emulsion, or from 12 to 40 minims for 1 pint.

For making from 1 to 5 gallons of emulsion, the apparatus known as the Morton patent egg-beater, or whisking machine, illustrated in Fig. 231, has been found very serviceable and satisfactory; it is made of heavily tinned iron, and supplied with a water chamber underneath, by means of which either hot or cold water may be employed for tempering, whenever desired. The upper tank is provided with a rounded bottom, and the emulsification is effected by means of several heavy wire beaters in circular form revolving rapidly in opposite directions within each other, whereby constant cross-cutting of the mixture and most perfect dashing of the constituents are insured; to prevent dust from entering, the tank is provided with a well fitting top. The beaters are easily removed by withdrawing the frame, and the apparatus can be quickly and thoroughly cleaned.

Another useful apparatus is the Hunter cyclone emulsifier (Fig. 232), which, like the Morton whisking machine, is intended to be operated by hand. It is provided with a porcelain-lined tank, has a capacity

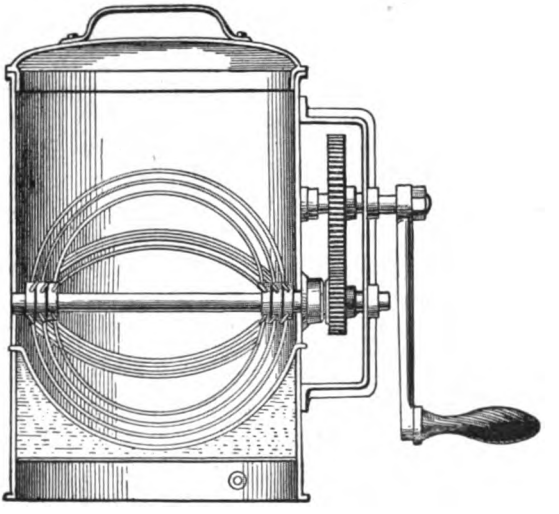


FIG. 231.—The Morton patent egg-beater.

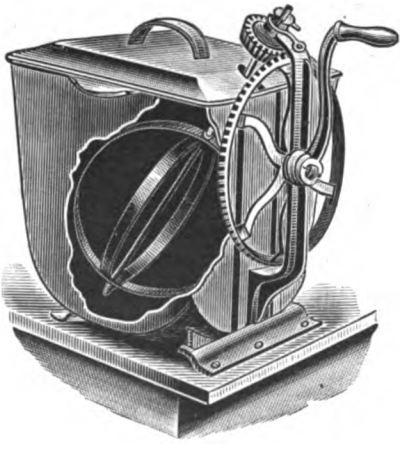


FIG. 232.—The Hunter cyclone emulsifier.

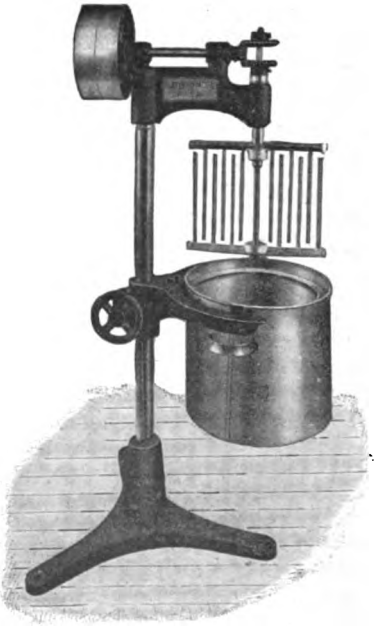


FIG. 233.—Stokes' emulsifier.

of 10 quarts, and can be firmly clamped to any bench or table. It is made by the J. H. Day Co., of Cincinnati, Ohio.

When emulsions are to be made on a large scale, the usual plan is to add the oil, in a thin continuous stream, to the mucilage contained in a suitable churning apparatus operated by steam power, the mixture being kept in constant agitation by rapidly revolving metallic blades or beaters moving through and in opposite directions to each other. In Figs. 233 and 234 are shown two styles of power emulsifiers made by the F. J. Stokes Machine Co., of Philadelphia, Pa., which can be had in different sizes ranging from 5 to 50 gallons' capacity. The tanks are built of heavy tin, copper, or galvanized iron and are provided

FIG. 234.—Variable speed emulsifier.

with faucets for drawing off the finished product. The emulsifier shown in Fig. 234 is provided with a speed controller, which oftentimes proves an important feature.

THE OFFICIAL EMULSIONS.

The Pharmacopœia recognizes 4 emulsions and the *National Formulary* 8; of these 8 are fixed oil emulsions, and 1 each an emulsion of volatile oil, of petrolatum, of a seed, and of a gum resin. With four exceptions, acacia is used as the emulsifying agent in all of these emulsions, and in each case specific directions for manipulation are given, which agree with those previously explained elsewhere. The following list shows their composition:

Latin name.	English name.	Composition.
Emulsum Amygdalæ U. S. P.	Emulsion of Almond	Made by triturating sweet almond, acacia, and sugar with water. Each mil. (or Cc.) represents 0.060 Gm. of almond.
Emulsum Asafœtidæ U. S. P.	Emulsion of Asafetida	Made by triturating gum-resin of asafetida with water. Each mil. (or Cc.) represents 0.040 Gm. of asafetida.
Emulsum Olei Morrhuæ U. S. P.	Emulsion of Codliver Oil	Made by emulsifying codliver oil with acacia and water, and adding to this syrup and methyl salicylate, and finally enough water to make up the required volume. Each mil. (or Cc.) represents 0.5 mil. (or Cc.) of codliver oil.
Emulsum Olei Morrhuæ cum Calcii Lactophosphate Nat. Form.	Emulsion of Codliver Oil with Calcium Lactophosphate	Made by emulsifying codliver oil with acacia and water, then adding a solution of calcium lactophosphate made with the aid of lactic acid, some flavoring and syrup of tolu, and finally enough water to make up the required volume. Contains 50 per cent. of codliver oil.
Emulsum Olei Morrhuæ cum Calcii Phosphate Nat. Form.	Emulsion of Codliver Oil with Calcium Phosphate	Made by emulsifying codliver oil with acacia and water, then adding some flavoring and a mixture of precipitated calcium phosphate and syrup of tolu, and finally enough water to make up the required volume. Contains 50 per cent. of codliver oil.
Emulsum Olei Morrhuæ cum Extracto Malti Nat. Form.	Emulsion of Codliver Oil with Extract of Malt	Made by emulsifying codliver oil with tragacanth and water, finally adding extract of malt in divided portions. This emulsion contains 30 per cent. by volume of codliver oil and about 50 per cent. of extract of malt.
Emulsum Olei Morrhuæ cum Hypophosphitibus Nat. Form.	Emulsion of Codliver Oil with Hypophosphites	Made by emulsifying codliver oil with acacia and water, then adding flavoring and syrup, a solution of the hypophosphites of calcium, sodium, and potassium, and finally enough water to make up the required volume. Each mil. (or Cc.) contains 0.5 mil. (or Cc.) of codliver oil.
Emulsum Olei Morrhuæ cum Pruno Virginiana Nat. Form.	Emulsion of Codliver Oil with Wild Cherry	Made by emulsifying codliver oil with acacia and water, then adding some flavoring, a mixture of fluidextract of wild cherry and syrup of tolu, and finally enough water to make up the required volume. Each mil. (or Cc.) contains about 0.5 mil. (or Cc.) of codliver oil.
Emulsum Olei Morrhuæ cum Vitello Nat. Form.	Emulsion of Codliver Oil with Egg	Made by emulsifying codliver oil with glycerite of yolk of egg and water, then adding some flavoring, syrup of tolu, and sufficient water to make up the required volume. Contains 50 per cent., by volume, of codliver oil.

Latin name.	English name.	Composition.
Emulsum Olei Ricini Nat. Form.	Emulsion of Castor Oil	Made by emulsifying castor oil with acacia and water, then adding syrup and tincture of vanilla, and finally enough water to make up the required volume. This emulsion contains about one-third its volume of castor oil.
Emulsion Olei Terebinthinæ U. S. P.	Emulsion of Oil of Turpentine	Made by emulsifying a mixture of rectified oil of turpentine and expressed oil of almond with acacia and water, then adding syrup and finally enough water to make up the required volume. Each mil. (or Cc.) contains 0.15 mil. (or Cc.) of rectified oil of turpentine.
Emulsum Petrolati (Emulsum Petrolei) Nat. Form.	Emulsion of Petrolatum	Made by emulsifying a mixture of white petrolatum and expressed oil of almond with acacia, tragacanth, and water, then adding syrup, tincture of lemon peel, and enough water to make up the required volume. Each mil. (or Cc.) contains 0.225 Gm. of white petrolatum.

SPECIAL REMARKS.

Emulsion of Almond.—The Pharmacopœia directs the blanched almonds, acacia, and sugar to be thoroughly mixed and then incorporated with the water. This is best done by first making a smooth paste with a small quantity of water, and then gradually diluting with the remainder of the water, so that a uniform liquid may result.

The acacia and sugar prescribed in the official formula are by no means essential to the formation of a perfect emulsion, although they add to the stability of the preparation. Emulsion of almond more closely resembles cow's milk in appearance than any other seed or oil emulsion made; the fixed oil present is kept suspended in a very fine state of division by means of the albuminous matter known as emulsin or synaptase, which constitutes the chief body of the seed. Blanched almonds should always be used, so that a pure white liquid may result. Almonds are best blanched by macerating them in warm water until the skin becomes loose, when it can be quickly removed by simple pressure between the fingers. Emulsion of almond is also known as *milk of almond*, and should always be made fresh when wanted. When intended as a solvent or vehicle for local applications, such as mercuric chloride, borax, zinc oxide, etc., it must invariably be made without the sugar and acacia directed in the official formula.

Emulsion of Asafetida.—As already stated on page 363, only select tears of the gum-resin should be used for this emulsion. These are crushed into a moderately coarse powder and beaten into a perfectly smooth paste with a very small quantity of water, after which more water is gradually added, so as to enable the operator to produce a

perfectly homogeneous mixture. In order to accomplish this it is necessary that the paste first obtained be scraped from the pestle and sides of the mortar and gradually reduced to a syrupy consistence by the use of small quantities of water. After straining the finished product through a previously moistened piece of flannel, only extraneous matter, such as sand, woody fiber, etc., should be left behind, but no particles of the gum-resin. Emulsion of asafetida is also known as milk of asafetida, and is sometimes prescribed by physicians as *lac asafœtidæ*. The color of the emulsion is usually white, but may be yellowish, pink, or even reddish, dependent upon coloring matter unavoidably present in the gum-resin.

The other official emulsions do not require special comment, except to state that in the case of the Emulsion of Oil of Turpentine the preparation is rendered more stable by the addition of the fixed oil. If the official directions for preparing the emulsions are strictly followed, satisfactory products will be obtained in every instance. Whenever solutions of salts are to be mixed with emulsions, they should be added after the primary emulsion has been properly diluted. The same precaution applies to the addition of syrup and tinctures.

CHAPTER XXVII.

MIXTURES.

THE term "mixture" in pharmacy, and more particularly in dispensing operations, is applied to liquid medicines which either contain insoluble substances in suspension or are composed of two or more liquids, with or without the addition of saline or other material in solution; in its more restricted application the term is applied to such medicines as are intended for internal administration. In only a few cases, in which the stability of the preparation for a considerable length of time can reasonably be assured, are mixtures kept in stock; hence the extemporaneous preparation of mixtures is a matter of constant occurrence, as it is with physicians a favorite method of administering medicines, because more extended use can be made of excipients and flavoring agents, with a view of improving the mixture pharmaceutically and therapeutically. Considerable skill and judgment are frequently necessary in the preparation of mixtures, so that the object of the prescriber may be fully attained and each fraction of the mixture contain an aliquot part of all the ingredients. All insoluble or only partly soluble substances, particularly those of a vegetable nature, should be brought to the condition of smooth and uniform suspension by trituration in the form of very fine powder with the liquid in the mortar; this is best done by first rubbing into a smooth paste with a portion of the liquid and then diluting this with the remainder, constantly stirring. Calcined magnesia or magnesia and charcoal can best be brought into a uniform mixture with water, by stirring at once with sufficient water to overcome the tendency of the magnesia to "set" in a gelatinous mass; a *small* quantity of water added to calcined magnesia also causes it to become gritty and difficult to mix. Some prefer to add the magnesia to the water and diffuse by agitation. In all cases the mixture should be passed through a loosely textured cloth. All powerful remedies, such as mercuric chloride, arsenic trioxide, the salts of morphine, strychnine, etc., should always be brought to a state of perfect solution before they are added to the other ingredients of a mixture, so as to insure a uniform distribution throughout the liquid. Substances which are readily diffusible in the liquid by agitation of the bottle do not, as a rule, require the addition of an excipient to insure their uniform suspension; but other insoluble substances which are relatively much heavier than water, or are inclined to float on the surface of the liquid, demand the addition of some mucilaginous or other body to increase the density. Syrup, glycerin, or honey is frequently preferable to

acacia or tragacanth, especially in the case of heavy metallic salts, liable to form, with the gum, a compact mass, which cannot be readily suspended by agitation.

Formerly emulsions were recognized among the mixtures, but they are now considered as a distinct class of preparations, the characteristics of which have been described in the preceding chapter.

In connection with the preparation of mixtures, it becomes necessary to consider the subject of incompatibility; this term is applied to the antagonism or disability of harmonious coexistence, which is exhibited by numerous substances when brought into contact with certain other substances. Liquids which are not mutually intersoluble, although they can be brought into homogeneous mixture with the aid of excipients, are often said to be incompatible with each other, as in the case of fixed oils and water, chloroform and glycerin, etc.; but, strictly speaking, the term incompatibility in pharmacy refers to the relation existing between two or more bodies by reason of which they cannot be mixed without undergoing or producing some change of a physical or chemical nature. Three kinds of incompatibility exist—pharmaceutical, chemical, and therapeutic—of which the pharmacist must take note, and for the proper understanding of which he must rely upon his knowledge of the physical, chemical, and medical properties of drugs.

Pharmaceutical Incompatibility.—Pharmaceutical incompatibility is such as affects the physical properties of substances, and is chiefly confined to their solubility; it may result in the partial or total separation of matter held in solution, which may include valuable constituents of the mixture, or it may cause simply a separation of liquids from each other. The changes due to pharmaceutical incompatibility, being entirely of a physical character, can often be avoided or overcome by judicious manipulation or by the addition of some suitable excipient or protective agent. The mixture of strongly alcoholic liquids with solutions of acacia—of acid or neutral aqueous liquids with resinous tinctures—of alcoholic or ethereal solutions of volatile oils and other substances with aqueous liquids—the admixture of solids which undergo liquefaction by reason of intersolubility, as in the case of camphor with solid fats, hydrated chloral, thymol, salol, menthol, etc. —the addition of certain metallic salts to vegetable solutions, causing gelatinization, as in the case of tincture of ferric chloride and mucilage of acacia—are all instances of pharmaceutical incompatibilities. In many cases of physical incompatibility the trouble may be averted by appropriate dilution before mixing, as, for instance, when spirit of nitrous ether or tincture of ferric chloride is to be mixed with a strong mucilage or acacia; a perfectly uniform mixture, free from precipitate or gelatinization, can be prepared if the mucilage as well as the spirit of tincture be first largely diluted with water, and such should be the invariable rule when these substances are prescribed together. When the tinctures of asafetida, guaiac, lupulin, myrrh, and

similar substances are placed in combination with aqueous saline liquids, separation of the resinous matter will invariably result unless a protective agent is present, by means of which the finely divided precipitate is kept in perfect suspension.

The value of honey as a preventive of unsightly precipitation may be exemplified in the following well known prescription, which has caused some pharmacists much annoyance:

℞—Potassii Chloratis . . . . . ℥j.
Tinct. Guaiaci
Tinct. Cinchonæ Co. } . . . . . āā ℥ss.
Mellis
Aquæ . . . . . q. s. ad ℥iij.—M.

If the honey be put into a mortar and the tincture of guaiac slowly added so that the two become well mixed, no separation of resinous matter will occur when the potassium chlorate dissolved in 1½ fluid-ounces of water is added with constant stirring; the compound tincture of cinchona is added lastly, and a uniform mixture of pink color results. If, on the other hand, the honey be mixed with the solution of potassium chlorate and a mixture of the two tinctures then added, trouble is sure to arise, as also if the honey be mixed with the two tinctures in a bottle and the solution of potassium chlorate then added.

Syrups, honey, and glycerin are frequently associated with resinous tinctures by physicians, for the purpose of avoiding the separation of resin, and, if used in sufficient quantity, will answer the purpose; in the absence, however, of such provision, it is the duty of the pharmacist to add some inert substance which will enable him to prepare a mixture of uniform composition. If the following two prescriptions be dispensed exactly as ordered, the resin of the tincture in both cases would be precipitated and gradually deposited on the sides and bottom of the bottle, thus depriving the patient of an important part of the medicine; no amount of shaking will even temporarily suspend the precipitated resin uniformly, but only increase its separation from the liquid.

℞—Potassii Bromidi . . . . . ℥iv.
Tinct. Lupulini . . . . . ℥j.
Aquæ Menthæ Vir. . . . . ℥ij.—M.

℞—Potassii Chloratis . . . . . ℥ij.
Tinct. Guaiaci . . . . . ℥j.
Aquæ . . . . . q. s. ad ℥iv.—M.

By mixing the resinous tincture or fluidextract with powdered tragacanth in a mortar, and then adding the water or saline solution gradually, with constant stirring, a perfect mixture can be obtained from which the suspended resin separates very slowly in a finely divided form, so as to be readily reincorporated by simple agitation. The proportion of tragacanth to be used will depend, to some extent, upon the volume of dilution; for instance, in the above prescriptions,

10 or 12 grains will be amply sufficient, while if a 6 oz. mixture were intended, 15 or 18 grains would be preferable. As a rule 10 grains of tragacanth will be required for each fluidounce of a tincture or half-fluidounce of a fluidextract.

This general rule to suspend the precipitated resinous matter by means of tragacanth should not be adhered to, however, in all cases, as, for instance, when a cosmetic lotion containing tincture of benzoin, glycerin, and water, is desired, or in the case of a mouth-wash composed of tincture of myrrh and water. In both mixtures the presence of tragacanth would prove decidedly objectionable, and very satisfactory results can be obtained by pouring the respective tincture slowly and in a thin stream into cold water contained in a bottle, adding any glycerin that may have been ordered, and mixing the ingredients by repeatedly and slowly inverting the bottle. The resinous matter in such cases is precipitated in a finely divided form and remains well suspended in the fluid. Strong agitation would cause rapid separation in lumps.

Other cases of physical incompatibility may be observed when strong solutions of metallic salts are to be made with aromatic waters; for instance, potassium or sodium bromide with camphor water or peppermint water, etc. Part of the camphor or oil of peppermint will be precipitated, and a remedy for the trouble may be found either in the use of plain distilled water or of a small quantity of alcohol for a corresponding amount of the medicated water, but such changes should never be made without consulting the prescriber. A solution of potassium bromide ʒj and camphor water ʒiv will require ʒiiss-ʒiij of alcohol, which is preferably added to sufficient camphor water to make a volume of 4 fluidounces, before dissolving the potassium salt.

The turbidity caused by the partial separation of volatile oil or other bodies when an alcoholic solution of the same is added to aqueous fluids is due to the decreased solubility of the substance in the diluted spirit, and cannot be overcome by the ordinary methods: filtration with the aid of such media as purified talcum, calcium phosphate, etc., is not always permissible, and then the application of the general rule—*never to dispense a mixture containing insoluble matter without a "Shake well before using" label*—is all that can be done by the pharmacist.

Sometimes the particular order of mixing two or more liquids will have a marked effect on the appearance of the finished product. Thus, in the preparation of the official aromatic spirit of ammonia, if the aqueous solution of ammonium carbonate be added to the alcoholic solution of the oils, as directed in the Pharmacopœia, a saline precipitate will almost invariably form, which subsequently is redissolved very slowly, often requiring days to produce a clear liquid. If, however, the alcoholic solution of the oils be added slowly to the watery alkaline solution, no precipitation whatever occurs.

Chemical Incompatibility.—Chemical incompatibility, as its name indicates, depends upon the chemical properties of substances, and invariably involves decomposition of one or all of the bodies brought into contact, with the resulting formation of new compounds. The existence of chemical incompatibility has proved most valuable in the study of inorganic and organic matter, and forms the basis upon which rests the very extensive superstructure of analytical chemistry. Chemical decomposition is not always accompanied by the separation of insoluble matter, for in numerous cases the newly formed compound is perfectly soluble in the liquid present. Among the most dangerous incompatibles are mixtures of the chlorates or permanganates with readily oxidizable substances; hence particular care must be exercised in bringing the former into intimate contact with organic matter, so as to avoid possible serious explosions.

There are different conditions under which chemical incompatibility manifests itself, chief among which are the following:

1. Two salts composed of different acid and basic radicals, when brought together in a state of solution, mutually decompose each other; the resulting new compounds may both remain in solution, in which case no evidence of decomposition is apparent, and it scarcely seems proper to consider the two salts used as incompatible with each other, as when solutions of ammonium chloride and potassium iodide are mixed, or those of cupric sulphate and zinc acetate. When, however, one of the new compounds is insoluble in the liquid and is deposited as a precipitate, true incompatibility has been established: as in the case of a mixture of solutions of lead nitrate and potassium iodide, lead iodide being precipitated. Sometimes the new insoluble compound enters into union and solution with one of the original substances, if the latter is present in excess, in which case the chemical incompatibility of the original two substances remains, and the resolution of the insoluble compound must be looked upon as a new operation. Such examples are presented by mercuric chloride and potassium iodide, if either salt is in excess, or by potassium cyanide and silver nitrate, the former salt being in excess.

2. Salts of the heavy metals, and, in many instances, also those of the alkaline earths and earths, are decomposed by the alkalies or their carbonates, forming insoluble compounds; hence incompatibility exists between such salts. As examples may be mentioned mercuric chloride with potassium hydroxide, lime water with sodium bicarbonate, calcium chloride with potassium carbonate, and alum with sodium carbonate.

Bismuth subnitrate is sometimes prescribed in an aqueous mixture with sodium bicarbonate, and almost invariably decomposition takes place, resulting in a more or less violent disengagement of carbon dioxide; as the reaction takes place slowly, at times it may not occur until the mixture has been transferred to a bottle and corked. The remedy lies either in using the bismuth subcarbonate in place of

the subnitrate, or in mixing the subnitrate and bicarbonate in a mortar and adding a little boiling water, so as to hasten and complete the reaction.

3. When oxidizing agents are brought into direct contact with organic matter chemical reaction at once ensues, which is often of a violent nature, and is among the most important incompatibilities met with. To this class belong the trituration of potassium chlorate with sulphur, sugar, tannin, or acacia; the solution of chromic acid or potassium permanganate with glycerin, etc.

4. The association of the salts of gold and silver with organic substances and other reducing agents gives rise to an exhibition of incompatibility by converting the gold and silver to the metallic state, thereby rendering them less soluble, as, for instance, when silver nitrate is dissolved in rose water instead of plain distilled water. All organic matter has a decomposing effect upon the compounds of gold and silver, but more particularly glucose, honey, syrup, and glycerin; hence these should be avoided in prescriptions.

5. Salts when brought in contact, either in the dry state or in solutions, with acids or bases stronger than their own acid or basic radicals, will suffer decomposition, the result being new compounds, with the evolution of the old acid or base, as in the preparation of the official solution of ammonium acetate. The decomposition of salts by stronger acids or bases is frequently resorted to intentionally, as in the well-known "Neutral Mixture," made from lemon juice and potassium bicarbonate, and in "Preston or Smelling Salts," composed of ammonium chloride and lime, usually flavored with oil of lemon and oil of lavender. In the former case it is desired to keep a large portion of the eliminated carbonic acid in solution, while in the latter the gradually liberated ammonia gas is the chief object sought.

Whenever carbonates are prescribed with an acid liquid the dispenser should allow the reaction to be completed before corking the vial, so that the greater portion of the gas may escape, and caution the patient to keep the vial in a cool place and not violently agitate it. If a viscid or saponaceous liquid is also to be added, as mucilage of acacia or syrup of senega, it is all the more important that chemical reaction be allowed to subside before the addition is made, and that as little carbon dioxide as possible be kept in the solution.

With some physicians, the following is a favorite prescription:

℞—Ammonii Carbonatis, Ammonii Chloridi . . . . . āā ʒj.
Syrupi Scillæ, Syrupi Senegæ . . . . . āā ʒj.
Syrupi Tolutani . . . . . ʒij.
Ft. sol.

The proper way of mixing these ingredients is to rub the salts to a fine powder, and add to them, *while in the mortar*, the syrups of squill and tolu previously mixed, stirring the mixture with the pestle *until effervescence ceases;* finally add the syrup of senega. If a per-

sistent froth forms on the surface of the liquid, this may be quickly dispelled by carefully sprinkling a few drops of alcohol over it before the mixture is transferred to a bottle.

To this class of incompatibilities belong also the decomposition and precipitation caused in fluidextract of licorice by acids; the sweet principle in licorice is ammonium glycyrrhizate, which, upon addition of dilute sulphuric or other acid, is decomposed, glycyrrhizin being deposited on the sides and bottom of the vessel. Physicians sometimes prescribe an acid solution of quinine together with fluidextract of licorice, in the hope of disguising the bitter taste, overlooking the fact that the bitter taste of quinine is always intensified by bringing the latter into solution. As the intended effect of the licorice is defeated by the presence of an acid, there is but one course open to the pharmacist with prescriptions of this kind, namely, to omit the acid, triturate the quinine with the fluidextract or syrup of licorice, and dispense the mixture with a "Shake well before using" label. It is advisable at the same time to explain to the physician what has been done, giving the reason therefore, so as to avoid, if possible, a repetition of the blunder.

6. The salts of the alkaloids are decomposed by certain salts of the alkalies, with the production of insoluble or sparingly soluble compounds; therefore such combinations require the special attention of pharmacists in order to guard against accidents. As a rule the alkali carbonates, iodides, and bromides are incompatible with alkaloidal salts, while the sulphates, nitrates, and chlorides appear to cause no trouble; hence in the case of the first-named salts the directions to shake the mixture should always be put on the bottle. The presence of a certain amount of alcohol in the liquid will prevent the precipitation of the newly formed alkaloidal salt, as may be demonstrated in the following prescription:

℞—Strychninæ Sulphatis . . . . . gr. j.
Potassii Bromidi . . . . . ʒj.
Aquæ destillatæ . . . . . q. s. ad ℥iv.
Ft. sol.

If the solution be prepared as written, strychnine bromide will gradually be deposited in colorless crystals, and may cause serious results should the same be retained in the bottle and a large quantity be taken with the last dose or two. If, however, equal volumes of aromatic elixir and water be used in place of water alone, no separation of strychnine bromide will occur. At least 12 per cent. of alcohol must be present in the solution to prevent precipitation.

In a few rare cases, when a sufficient quantity of solvent is present to take up the alkaloid in its pure state, it may be preferable to use the latter in place of its salt, as, for instance, in the following prescription:

℞—Codeinæ Sulphatis . . . . . gr. viij.
Potassii Bromidi . . . . . ʒj.
Aquæ destillatæ . . . . . q. s. ut ft. ℥iv.
Ft. sol.

It was found that if the codeine sulphate was used, as prescribed, a precipitate invariably formed, which was with difficulty uniformly suspended by agitation, but by using a corresponding quantity of the pure alkaloid codeine in place of the salt a permanently clear solution was obtained. Morphine sulphate is sometimes prescribed in conjunction with sodium bicarbonate, the result being a minutely crystalline precipitate. Quinine sulphate and potassium acetate should not be associated in solution, on account of the slight solubility of the quinine acetate, which is formed as a very bulky precipitate, and may cause solidification of the mixture.

7. Vegetable astringents are incompatible with alkaloids, glucosides, albumen, gelatin, and many metallic salts; in some cases curdy precipitates are formed, which afterward adhere to the sides of the vessels, while in other cases light, readily diffusible precipitates are obtained, or possibly only turbidity or discoloration ensues. The character of such a mixture depends to some extent upon the degree of dilution and the presence of other bodies. Quinine and tannin are sometimes prescribed together, but should never be triturated with water, as a tough, insoluble mass would at once be formed; the two substances are best mixed with syrup and afterward diluted with water, if desired, when the insoluble quinine tannate can be readily suspended by simple agitation. The formation of ink depends upon the incompatibility of tannin with iron salts, and is a fruitful source of annoyance to the pharmacist. The value of strong coffee and tea or similar astringent infusions as antidotes for metallic poisoning is due to the formation of sparingly soluble compounds. Vegetable astringents have been found incompatible also with spirit of nitrous ether, several explosions have occurred from mixing the latter with the fluidextracts of uva ursi, matico, geranium, and even gentian; the gas liberated by these reactions appeared heavily charged with some nitrous compound.

Spirit of nitrous ether unless free from acidity, which is rarely the case except in the freshly made article, is incompatible with solutions of alkali iodides and bromides, causing the liberation of iodine and bromine, respectively, as shown by the high color of the liquid. With solutions of antipyrine it gives rise to the formation of a green-colored compound, known as isonitroso-antipyrine, which, however, is not poisonous, as was formerly believed. Whenever spirit of nitrous ether, therefore, is to be dispensed in such mixtures, it should be first carefully neutralized with sodium or potassium bicarbonate; this will, however, not prevent the development of acid for all times, as the spirit of nitrous ether will gradually undergo decomposition in the presence of water.

The presence of certain protective agents has been known to avert, or at least to modify, chemical decomposition between some substances; in such cases it is, of course, essential that the protective agent be mixed with one of the substances before the other is added. The

following examples will show the action of glycerin, acacia, and syrup, in this respect. Physicians frequently prescribe cocaine hydrochloride or morphine salts in solution, together with borax, which causes precipitation and thus unfits the solution for use; the addition of a little glycerin prevents the decomposition. Zinc chloride and borax, prescribed together in solution, will cause the formation of insoluble zinc borate, which is prevented, however, by the presence of glycerin; strange to say, such a clear solution containing glycerin will bear further dilution with water only up to a certain point, beyond which precipitation ensues. The action of the glycerin in the foregoing cases is not clearly understood, but, reasoning from the effect of glycerin on borax alone, it may be assumed that a similar action obtains in the mixture with alkaloidal and other salts, the glycerin decomposing the borax by liberating a part of the boric acid, which itself is perfectly compatible with the salts above mentioned, as has been shown by making the solutions with boric acid, instead of borax or borax and glycerin. On the other hand, glycerin may sometimes act as a disturbing agent and cause decomposition which otherwise would not occur. Borax and sodium bicarbonate are perfectly compatible in aqueous solution, and are frequently prescribed together; if glycerin be present, reaction is set up by the boric acid liberated from the borax, and the sodium bicarbonate is decomposed with copious evolution of carbon dioxide. Such a mixture must be made in a mortar and the reaction allowed to subside before bottling it.

Corrosive mercuric chloride and lime water are known to be incompatible, but are often ordered together, with the view of utilizing the freshly formed yellow mercuric oxide in moist condition; mercuric chloride will also precipitate acacia from a strong solution, but if a dilute solution of mercuric chloride be added to mucilage of acacia and subsequently mixed with lime water, no precipitate whatever will occur for several days, when finally a grayish deposit of finely divided metallic mercury or mercurous oxide is formed. When a physician orders such a combination as mercuric chloride, water, mucilage of acacia, and lime water, the object is plainly to keep the mercuric oxide better suspended, and the mixture should be made by adding the mucilage last of all, after decomposition of the mercuric chloride has been completed.

Chemical incompatibility may result in rendering a mixture less active, or even inert, from the formation of insoluble compounds, as when tartar emetic is ordered in combination with syrup of wild cherry, or tincture of digitalis with tincture of cinnamon, etc.; on the other hand, the medicinal activity of the mixture may be intensified by the formation of poisonous compounds, as in the case of mercurous iodide with soluble iodides, producing mercuric iodide and metallic mercury, or the association of calomel with soluble chlorides or iodides, etc. In all such cases the pharmacist should consult the prescriber and acquaint him with the prospective results.

A well marked case of double incompatibility, both physical and chemical, is exhibited in the following prescription:

℞—Zinci Sulphatis	0.650	Gm.
Mucilaginis Acaciæ	30.0	Cc.
Aquæ destillatæ	90.0	Cc.
Liq. Plumbi Subacetatis	4.0	Cc.—M.

It is very evident that decomposition between the zinc and lead salts is desired, but the incompatibility existing between the mucilage of acacia and solution of lead subacetate must be overcome, and this can be done effectually by following a certain order of mixing. The zinc sulphate should be dissolved in the water and the solution of lead subacetate then added, which will cause a precipitate of lead sulphate to form; to this mixture the mucilage of acacia is added and the whole shaken—no precipitation of gum will occur, and the newly formed lead salt will remain well suspended.

It must not be supposed, however, that because precipitation occurs as a result of chemical incompatibility the mixture is always rendered inert thereby; the decomposition is often intentional with a view to obtaining the insoluble compound in a freshly formed and more active condition. Such instances are found in the well known "black wash" and "yellow wash" (prepared from lime water with calomel and corrosive sublimate, respectively), in the mixture of solutions of tannin and of lead subacetate, which produce a magma-like precipitate of lead tannate, and in the frequently prescribed mixture of zinc sulphate with a solution of lead acetate, containing freshly precipitated lead sulphate, which is much preferred. The compound iron mixture, formerly official, is another instance of intentional decomposition, the newly formed ferrous carbonate being the object sought. It requires no little judgment on the part of the pharmacist to discern when the prescriber intentionally orders chemically incompatible substances together, or when this happens from a want of familiarity with chemical reactions.

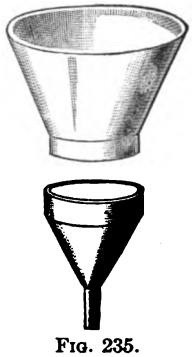


FIG. 235.

Therapeutic Incompatibility.—Therapeutic incompatibility depends entirely upon the antagonism existing between drugs in regard to their physiological effect or medical action, and does not properly belong to the domain of pharmacy; the remedy for such a condition lies solely in the hands of the physician, who is supposed to be familiar with the requirements of his patients and the therapeutic action of drugs. Sometimes the intended medicinal effect of a substance is destroyed by chemical action, as when ammonium carbonate is associated with syrup of squill; this, however, cannot be considered as a thereapeutic incompatibility.

While it is well understood in prescription practice that solutions should always be filtered through a pledget of cotton placed in the throat of a funnel to remove motes and specks, the rule should also prevail in dispensing mixtures that the mixture be strained through moderately coarse bolting-cloth, in order that the insoluble matter be free from lumps and in a uniformly divided state; the straining is best accomplished by placing the bolting-cloth between the upper and lower parts of a rubber or tin funnel, as shown in Fig. 235, which can be inserted directly into the prescription vial.

The subject of incompatibility is practically an endless one, and the reader is referred for further detailed information to two books that should be in every pharmacist's library, namely, Ruddiman's *Incompatibilities in Prescriptions* and Scoville's *Art of Compounding*. The following summary will, to some extent, aid the dispenser in determining the character of numerous mixtures; it must be borne in mind, however, as stated before, that not all incompatibles produce inert or poisonous compounds, and that while in many cases the incompatibility can be overcome by appropriate means, physicians frequently associate incompatible substances for a specific purpose.

SUMMARY OF INCOMPATIBILITIES. (After HAGER.)

Acacia	with ferric chloride, alcohol, borax, basic lead subacetate, ethereal tinctures.
Acids in general	" alkalies, alkaline fluids, acetates, and metallic oxides.
Acid, Arsenous	" lime water, magnesia, and oxides of iron.
Acid, Carbolic	" potassium permanganate, iodine, bromine, caustic alkalies, and iron salts.
Acid, Chromic	" glycerin, alcohol, ether, essential oils, and organic matter in general.
Acid, Picric	" alkaloidal salts, dry acids, iodine, sulphur, and organic salts. (These incompatibilities extend also to the salts of picric acid.)
Acid, Salicylic	" potassium permanganate, iron salts, lime water, potassium iodide, and soap. (These incompatibilities extend also to the salts of salicylic acid.) Alkali salicylates will darken unless an excess of acid be present.
Acid, Tannic	" mucilages, tartar emetic, silver nitrate, metallic salts in general, alkaloids and their salts, lime water, potassium chlorate, alkali carbonates and bicarbonates, albumen, gelatin, and chlorine water.
Albumen	" mineral acids, alcohol, mercuric chloride, and vegetable astringents.
Alkaloidal Salts	" borax, tannin, and all vegetable astringents, alkali carbonates, the permanganates, iodides, liquorice, strong mucilages, magnesium carbonate, and alkaline tinctures.
Alum	" alkalies and alkali carbonates.

SUMMARY OF INCOMPATIBILITIES. (After HAGER.)—*Continued.*

Ammonium Acetate Ammonium Bromide	with mineral acids, alkali carbonates, chlorine, potassium chlorate and dichromate, silver nitrate, mercurous chloride and nitrate.
Ammonium Chloride Ammonium Phosphate	" carbonates of the alkalies and earths.
Amyl Nitrite	" alcohol, tinctures in general, alkali carbonates, calomel, lead salts, potassium iodide, the bromides and ferrous salts.
Antimony, Sulphurated	" sodium bicarbonate, potassium bitartrate, bismuth subnitrate and calomel.
Antipyrine	" sodium salicylate (dry), calomel, chloral hydrate, and spirit of nitrous ether if acid.
Apomorphine Hydrochloride	" sodium carbonate and bicarbonate, iodine, tannin, and iron salts.
Barium Chloride	" sulphuric and phosphoric acids and their salts, carbonates, tartrates, vegetable infusions and medicinal wines.
Bismuth Subnitrate	" calomel, tannin, sulphur, and antimony sulphide.
Calcium Chloride	" calomel, sulphates, phosphates, tartrates and carbonates.
Calcium Hypophosphite	" potassium chlorate, iodide, and permanganate; also chlorinated lime. (These incompatibilities extend to all hypophosphites.)
Calomel (Mercurous Chloride)	" acids, acid salts, alkali carbonates, lime water, ammonium chloride, iodine, potassium iodide, ferrous chloride and iodide, sulphur, bitter almond water, cherry-laurel water, antimony sulphide, and antipyrine.
Chloral Hydrate	" water (slow decomposition), warm water, alkali carbonates and organic salts, calomel, potassium cyanide, antipyrine, salts of ammonium, mercurous nitrate, permanganates, alcohol, tinctures in general, bromides and iodides.
Chlorine Water	" alkalies and their carbonates, ammonium salts, salts of the organic acids, lead salts, silver nitrate, mucilages, tannin, extracts, tinctures, infusions, emulsions and milk.
Corrosive Sublimate (Mercuric Chloride)	" lime water, soap, iodine, opium, potassium iodide, organic acids, tannin, and alkali carbonates.
Digitalis	" tannin, lead acetate, iodine, potassium iodide, iron salts, and alkali carbonates.
Iodine	" ammonia, starch, metallic salts, fatty and volatile oils, emulsions, carbolic acid, chloral hydrate, acacia, tragacanth, magnesium carbonate, and sodium thiosulphate (hyposulphite).
Iodoform	" silver and other nitrates, potassium chlorate, nitrites, and mineral acids. (The modification or destruction of the odor of iodoform by the following substances points to incompatibility: tannin, Peru balsam, tincture of myrrh, naphtalene, cumarin, and the volatile oils of anise, bergamot, fennel, peppermint and turpentine.)
Iron, Reduced	" aloes, tannin, infusions, extracts, metallic and alkaloidal salts.
Iron Salts	" alkali carbonates and bicarbonates, mucilages, tannin, infusions, extracts and astringent tinctures.

SUMMARY OF INCOMPATIBILITIES. (After HAGER.)—*Continued.*

Lead Acetate (also Lead Subacetate)	with	opium, lime water, ammonium chloride, alum, potassium iodide, iodine, acacia, tragacanth, tannin, carbonates and sulphates, and sulphuric and hydrochloric acids. (Normal lead acetate is compatible with mucilage of acacia, but the basic or subacetate causes precipitates, even in minute quantities.)
Lime, Chlorinated	"	ammonium chloride, sulphur, tannin, metallic sulphides, glycerin, volatile oils and fatty substances.
Lime Water	"	acids, ammonium salts, carbonates, tartrates, metallic salts, tannin, infusions and many tinctures.
Morphine Salts	"	the salts of iron, manganese and silver, potassium chlorate and permanganate, nitrites and nitrates, carbonates of the alkalies and the earths, amyl nitrite and bitter-almond water.
Musk	"	acids, acetates, tannin, ergot and metallic salts.
Opium, including the Tincture and Extract of Opium	"	alkali carbonates, tannin, metallic salts, iodine, chlorine water, and the preparations of nux vomica and belladonna.
Pepsin	"	alkaline substances, alcohol and tinctures in general.
Potassium Bromide	"	mineral acids, chlorine water, and the salts of mercury and silver.
Potassium Chlorate	"	mineral acids, tannin, catechu, sulphur, charcoal, calomel, sulphites, ferrous salts, nitrites, hypophosphites, sugar, honey and vegetable powders.
Potassium Iodide	"	acids and acid salts, alkaloidal salts, silver nitrate, ferric salts, potassium chlorate, spirit of nitrous ether (if acid) and salts of lead and mercury.
Potassium Permanganate	"	fatty and volatile oils, alcohol, glycerin, ammonia and ammonium salts, alkaloids, sulphur, charcoal and organic substances in general.
Silver Nitrate	"	hydrochloric, sulphuric, acetic, and tartaric acids and their salts, hydrocyanic acid, iodine, potassium iodide and bromide, antimony, carbonates of the earths and astringent tinctures.
Sodium Bicarbonate	"	acids and acid salts, tannin, metallic and alkaloidal salts.
Tartar Emetic	"	acids and alkalies, calomel, tannin, soap, acacia, opium and vegetable astringents.

In Europe, effervescing mixtures are often prescribed under the name "Saturations," which are made by adding to lemon juice, vinegar, or tartaric or citric acid solution, sufficient of an alkali carbonate to produce a neutral or nearly neutral salt, the liquid retaining in solution a large portion of the carbon dioxide evolved, which adds materially to the refreshing taste of the mixture. The Pharmacopœia of 1900 (VII Rev.) published complete tables of the quantity of different alkalies and alkali carbonates necessary to neutralize 100 parts of the various official acids.

THE OFFICIAL MIXTURES.

Of the 2 preparations recognized as mixtures in the Pharmacopœia, only 1 can be kept on hand for several days or longer in warm weather; the other should be freshly made when needed.

TABLE OF THE OFFICIAL MIXTURES.

Latin name.	English name.	Proportion of ingredients.
Mistura Cretæ	Chalk Mixture	Comp. Chalk Powder 200 Gms., Cinnamon water 400 mils. (or Cc.), Water sufficient to make 1000 mils. (or Cc.).
Mistura Glycyrrhizæ Composita	Compound Mixture of Glycyrrhiza (Brown Mixture)	Pure Extract of Glycyrrhiza 30 Gms., Granulated Acacia 30 Gms., Syrup 50 mils. (or Cc.), Antimony and Potassium Tartrate 0.240 Gm., Camphorated Tincture of Opium 120 mils. (or Cc.), Spirit of Nitrous Ether 30 mils. (or Cc.), Water sufficient to make 1000 mils. (or Cc.).

Although not officially designated as mixtures, the two following chemical preparations may be considered as such. The suspension of the precipitated respective compounds is not absolutely permanent, but is readily reëstablished by simple agitation.

Latin name.	English name.	Composition.
Magma Bismuthi	Bismuth Magma (Milk of Bismuth)	An aqueous suspension of bismuth hydroxide, containing about 6 per cent. of the latter, together with a small quantity of bismuth subcarbonate.
Magma Magnesiæ	Magnesia Magma (Milk of Magnesia)	An aqueous suspension of magnesium hydroxide, containing about 7 per cent. of the latter compound.

The *National Formulary* gives directions for the preparation of the following mixtures, some of which have been known as proprietary or semiproprietary preparations for many years, and others are identical with preparations of the same name, officially recognized in former or present foreign pharmacopœias:

Latin name.	English name.	Composition.
Mistura Astringens	Astringent Mixture	Made by adding solution of lead subacetate to a solution of copper and zinc sulphates in diluted acetic acid. This preparation is also known as Villate's Mixture.
Mistura Ammonii Chloridi	Mixture of Ammonium Chloride	Made by dissolving ammonium chloride and purified extract of licorice in water. This mixture is sometimes designated as Mistura Solvens Simplex.
Mistura Camphoræ Acida	Acid Camphor Mixture	Made by adding nitric acid and tincture of opium to camphor water. It was formerly often prescribed as Mistura Antidysenterica or Hope's Mixture.

Latin name.	English name.	Composition.
Mistura Camphoræ Aromatica	Aromatic Camphor Mixture	Made by adding compound tincture of lavender to a solution of sugar in camphor water. Also known as Parrish's Camphor Mixture.
Mistura Carminativa	Carminative Mixture	Made by triturating the oils of caraway, fennel, and peppermint with magnesium carbonate and water; then adding potassium carbonate, syrup and tincture of opium, and finally sufficient water to make up the desired volume. This popular preparation, better known as Dalby's Carminative, contains in each fluidounce 12 minims of tincture of opium, representing about 1 grain of powdered opium.
Mistura Chlorali et Potassi Bromidi Composita	Chloral and Bromide Compound	Made by treating a mixture of the extracts of cannibis and hyoscyamus in the presence of finely powdered pumice with an aqueous solution of hydrated chloral and potassium bromide during 24 hours; then filtering and passing enough water through the filter to make up the required volume.
Mistura Chloroformi et Morphinæ Composita	Compound Mixture of Chloroform and Morphine (Chloroform Anodyne)	Made by adding chloroform, ether, tincture of cannabis and tincture of capsicum to a solution of oil of peppermint in alcohol; then adding a solution of morphine sulphate in water and glycerin, and finally enough alcohol to make up the required volume. Each mil. (or Cc.) contains 0.125 mil. (or Cc.) of chloroform and 0.0025 Gm. of morphine sulphate. This mixture has also been designated Chloroform Anodyne.
Mistura Copaibæ	Lafayette Mixture	Made by mixing copaiba, solution of potassium hydroxide, spirit of nitrous ether, syrup, mucilage of acacia, and compound tincture of lavender.
Mistura Copaibæ et Opii	Chapman's Mixture	Made by mixing copaiba, mucilage of acacia, tincture of opium, compound tincture of lavender, spirit of nitrous ether, and water.
Mistura Ferri Composita	Compound Iron Mixture (Griffith's Mixture)	Made by emulsionizing myrrh with rose water with the aid of potassium carbonate and sugar, adding spirit of lavender and finally a solution of ferrous sulphate in rose water.
Mistura Guaiaci	Mixture of Guaiac	Made by mixing tincture of guaiac, and honey with cinnamon water.
Mistura Magnesiæ, Asafœtidæ et Opii	Mixture of Magnesia, Asafetida and Opium (Dewees' Carminative)	Made by triturating magnesium carbonate and sugar with tincture of asafetida and tincture of opium, and adding sufficient water to bring the volume up to the required amount.

Latin name.	English name.	Composition.
Mistura Olei Picis	Mixture of Oil of Tar	Made by adding oil of tar to a warm solution of purified extract of licorice and sugar and allowing the mixture to cool in a covered vessel; chloroform and oil of peppermint dissolved in alcohol are then added and enough water to make up the required volume. This preparation is also known as Mistura Picis Liquidæ or Tar Mixture.
Mistura Oleo-Balsamica	Oleo-Balsamic Mixture	Made by dissolving Peru balsam and the oils of lavender, thyme, lemon, nutmeg, and cinnamon in alcohol. This solution is practically identical with the Mixtura Oleoso-Balsamica of the German Pharmacopœia, which is also known as Balsamum Vitæ Hoffmanni.
Mistura Opii et Chloroformi Composita	Compound Mixture of Opium and Chloroform (Squibb's Diarrhœa Mixture)	Made by mixing tincture of opium, tincture of capsicum, spirit of camphor and chloroform with alcohol. Each fluidrachm contains 12 minims of tincture of opium.
Mistura Opii et Rhei Composita	Compound Mixture of Opium and Rhubarb (Sun Cholera Mixture)	Made by mixing tincture of opium, tincture of capsicum, tincture of rhubarb, spirit of camphor and spirit of peppermint with alcohol. Each fluidrachm contains 12 minims of tincture of opium.
Mistura Opii et Sassafras (Mistura Opii Alkalina)	Mixture of Opium and Sassafras (Godfrey's Cordial)	Made by dissolving potassium carbonate in water, adding to this syrup and tincture of opium, and finally a solution of oil of sassafras in alcohol. Each fluidrachm contains 2.1 minims of tincture of opium.
Mistura Pectoralis, Stokes	Stokes' Expectorant	Made by adding an aqueous solution of ammonium carbonate to a mixture of fluidextract of senega, camphorated tincture of opium, and fluidextract of squill; finally sufficient syrup of tolu is added to make up the required volume.
Mistura Rhei Alkalina (Syrupus Rhei et Potassii Compositus)	Alkaline Mixture of Rhubarb (Neutralizing Cordial)	Made by dissolving potassium carbonate in syrup, then adding fluidextract of rhubarb, fluidextract of hydrastis, tincture of cinnamon and spirit of peppermint, and sufficient diluted alcohol to bring the volume up to the required amount.
Mistura Rhei Composita	Compound Mixture of Rhubarb	Made by adding the fluidextracts of rhubarb and ipecac and glycerin to a solution of sodium bicarbonate in peppermint water. This preparation is also known as Mixture of Rhubarb and Soda.

SPECIAL REMARKS.

Magma Bismuthi (*Bismuth Magma*, also known as *Milk of Bismuth*).—This preparation, which has at times also been called *Cream of Bismuth*, is made by adding an acidulated solution of bismuth trinitrate, rapidly and with constant stirring, to a mixed solution of ammonium carbonate and ammonia water. As a result of chemical reaction bismuth hydroxide and bismuth subcarbonate are formed, the latter in small quantity, and remain suspended in the water; repeated washing by decantation and on a strainer removes the ammonium nitrate and excess of alkali.

Bismuth magma is a thick, white liquid of neutral reaction. The Pharmacopœia requires that when dried and ignited, it shall yield not less than 5.6 per cent., nor more than 6.2 per cent. of bismuth oxide.

Magma Magnesiæ (*Magnesia Magma*, also known as *Milk of Magnesia*).—This is directed to be made by adding a solution of sodium hydroxide to an aqueous suspension of the magnesium carbonate, with constant stirring, and then agitating the mixture frequently during 15 minutes. The reaction results in the precipitation of magnesium hydroxide in the form of a magma, which latter is repeatedly washed with distilled water, until the red color produced in 50 mils. (or Cc.) of the washings by 3 drops of phenolphthalein test-solution is discharged upon addition of 1 drop of diluted sulphuric acid. The magma is then allowed to settle down to the required volume.

The Pharmacopœia permits the addition of 0.5 mil. (or Cc.) of oil of peppermint, or oil of anise or other suitable flavoring agent to 1000 mils. (or Cc.) of the magma, and requires that the finished product, when assayed, shall be shown to contain not less than 6.5 per cent., nor more than 7.5 per cent. of magnesium hydroxide.

The amount of water ordered in the official formula for suspension of the magnesium carbonate appears insufficient, since the newly formed magma of magnesium hydroxide fails to separate sufficiently to permit decantation of the mother liquor. In the author's experience the use of nearly twice as much water for the magnesium carbonate yields better results, and subsequent washing of the magma by decantation is materially facilitated.

Milk of magnesia occurs as a thick, white, somewhat opalescent liquid, which should be preserved in wide-mouthed bottles, tightly stoppered with corks previously dipped in melted paraffin, in order to prevent the absorption of carbon dioxide from the air and consequent change of a part of the magnesium hydroxide into carbonate.

Mistura Cretæ (*Chalk Mixture*).—The compound chalk powder directed for this preparation is the official powder composed of 3 parts of prepared chalk, 2 parts of acacia, and 5 parts of sugar, the insoluble chalk being kept in suspension by the gum and sugar in solution.

Precipitated calcium carbonate must not be used in making this mixture, as it is crystalline and does not make so smooth a preparation, nor remain so perfectly in suspension as the prepared chalk. Chalk mixture should be made in small quantities and kept in a cold place.

Mistura Glycyrrhizæ Composita (*Compound Mixture of Glycyrrhiza, or Compound Licorice Mixture*).—This well known preparation, popularly called Brown Mixture, is made by dissolving the pure extract of licorice and acacia in 500 mils. (or Cc.) of water and then adding the other ingredients in the order named in the formula, the antimony and potassium tartrate being dissolved in 12 mils. (or Cc.) of water, and the required volume of finished product being obtained by the addition of sufficient water. The resulting mixture is rather an unsightly preparation, and not in keeping with modern elegant pharmacy; it may be improved in appearance by setting it aside for a couple of days with frequent agitation, then filtering. The formula suggested by Charles Tilyard, in 1860, yields an equally efficient and far handsomer preparation; it prescribes a larger proportion of sugar (by no means a disadvantage), and can be improved still further by the use of purified extract of licorice, as now ordered by the Pharmacopœia. The formula, as modified and adapted to the porportions of the Pharmacopœia, is as follows: Dissolve 30 Gms. of pure extract of licorice in 300 mils. (or Cc.) of water: add 120 mils. (or Cc.) of camphorated tincture of opium, and 30 mils. (or Cc.) of spirit of nitrous ether, and set the mixture aside for twelve or twenty-four hours, with occasional agitation; filter the liquid into a bottle containing 30 Gms. of granulated acacia and 600 Gms. of granulated sugar, add 0.240 Gm. of antimony and potassium tartrate dissolved in 12 mils. (or Cc.) of distilled water, and wash the filter with sufficient water to bring the volume of the finished product up to 1000 mils. (or Cc). The sugar and acacia are readily dissolved by agitation, the result being a thin rich-looking, clear syrup which keeps admirably.

CHAPTER XXVIII.

PILLS.

PILLS are a very convenient mode of administering medicine, the chief advantages lying in the small bulk to which the medicine is reduced and the almost complete disguise of bitter and nauseous remedies, by reason of their being swallowed without previous mastication. Pills are admirably adapted for the administration of heavy metallic substances not readily suspended in liquids, and also in cases in which the action of the medicine is to be slow, or even retarded until it reaches the lower bowel. The usual shape given to pills is that of a sphere or globe, although an ovoid shape is also sometimes used, and, in a few cases, even the lenticular shape is preferred. Their weight ranges from less than 0.06 Gm. to 0.3 Gm. (1 gr. to 5 gr.) for vegetable substances, or about 0.5 or 0.6 Gm. (8 to 10 grains) for heavy mineral compounds; small pills weighing less than 0.06 Gm. (1 grain) but more than 0.02 Gm. ($\frac{1}{3}$ grain) are termed *granules*, and those weighing less than 0.02 Gm. ($\frac{1}{3}$ grain) are known as *parvules*. When a pill exceeds 0.65 Gm. (10 grains) in weight, it is usually called a *bolus*. Boluses are occasionally made weighing 1.3 to 2.0 Gms. (20 to 30 grains) each, and are often of a softer consistence than pills.

Although of late years the extemporaneous preparation of pills has materially decreased, and in some localities is almost unknown, the operation must yet be considered one of the most important pharmaceutical manipulations, and is deserving of a lengthy discussion, because the opportunities for a practical acquaintance with the details of the work are growing less day by day, owing to the untiring efforts of manufacturers to induce physicians to specify factory-made pills in their prescriptions.

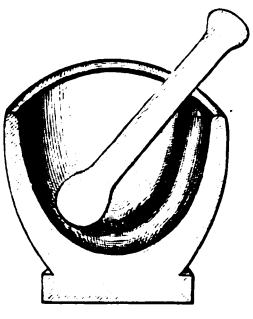
The most important step in the preparation of pills is the formation of a proper mass, which should consist of a paste sufficiently plastic to admit of being moulded without adhering to the mould, yet firm enough to prevent the pills from losing their original shape. Although a firm consistence should characterize every well made pill mass, its ready disintegration and solution in the fluids of the stomach and bowels are of paramount importance, and it is essential to so unite the ingredients of a pill mass that ready separation in the stomach may be assured. Plasticity is that peculiar condition in which adhesiveness and firmness are properly balanced; the former of these properties is due to a partial softness, which enables the particles of the mass to adhere to one another, thus imparting tenacity to the whole. Some

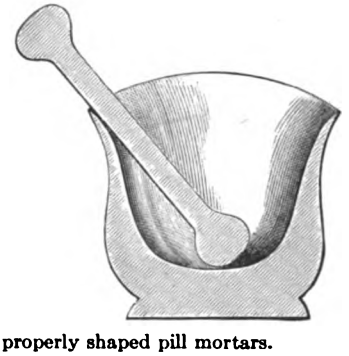
substances possess this adhesiveness in themselves, but require the addition of a liquid—water or alcohol—in order to develop it; as, for instance, gums and resinous drugs. Other substances possess no inherent adhesive properties, and in such cases it becomes necessary to impart tenacity to them by the addition of some adhesive liquid or solid material; such substances are camphor, calomel, bismuth salts, some saline or vegetable powders, reduced iron, and the like. Firmness in a pill mass is as essential as adhesiveness, and while the latter is brought about by a state of partial solution or fluidity, yet, inversely, the insolubility of some particles is necessary for the required firmness. The substances added to pill masses as adhesive or absorbent agents are known as excipients, and must be employed judiciously, so that the constituents of the mass be not modified in their action nor the bulk unnecessarily increased. After each addition of excipient the mass should be well kneaded, which, itself having a softening influence by reason of the heat generated, enables the operator to judge of the condition of the mixture. Whenever possible, all constituents of a pill mass should be reduced to very fine powder before the addition of any excipient, as only in this condition can the homogeneity of the mass, as well as the subsequent accurate division of doses, be assured. Small quantities of potent remedies, such as alkaloids, narcotic extracts, toxic chemicals, etc., are preferably triturated with a little sugar of milk before mixing them with the other ingredients, to facilitate uniform distribution.

Whenever substances are ordered in a pill mass in quantities which it is impossible or inconvenient to weigh accurately, as, for instance, aconitine 0.004 Gm., digitalin 0.012 Gm., atropine sulphate 0.020 Gm., veratrine $\frac{1}{24}$ grain, strychnine $\frac{1}{12}$ grain, morphine sulphate $\frac{1}{6}$ grain, etc., a dilution of the substance should be made with sugar of milk in such proportions that a conveniently weighable quantity shall contain the desired amount of the active ingredient. Thus, if 0.004 Gm. of any substance is wanted, carefully triturate 0.050 Gm. of the substance with 0.450 Gm. of sugar of milk (or 0.100 with 0.900 Gm. if more convenient); each 0.010 Gm. of the mixture will then contain $\frac{1}{50}$ of 0.050, or 0.001 Gm. of the medicinal agent, and hence 0.040 Gm. will contain 0.004 Gm., or 0.120 Gm. will contain 0.012 Gm., or 0.200 Gm. will contain 0.020 Gm., etc. If $\frac{1}{24}$ of a grain of any substance is needed, triturate $\frac{1}{2}$ grain of it with $11\frac{1}{2}$ grains of sugar of milk (or 1 grain with 23 grains if more convenient), and each grain of the mixture will contain $\frac{1}{24}$ grain of the active ingredient, or $1\frac{1}{2}$ grains will contain $\frac{1}{16}$ grain, or 2 grains will contain $\frac{1}{12}$ grain, or 3 grains will contain $\frac{1}{8}$ grain, or 4 grains will contain $\frac{1}{6}$ grain, or 6 grains will contain $\frac{1}{4}$ grain, etc. In a similar manner other dilutions may be made to obtain a different number of milligrammes or different fractions of a grain. The proper procedure for making these dilutions, is to place a small quantity of sugar of milk in a mortar, add the drug, triturate thoroughly and then add the remainder of the sugar of milk in divided portions,

scraping the mixture well from the pestle and mortar and triturating thoroughly after each addition. In this way more perfect distribution of the drug will be effected, so that any fraction of the mixture will represent an aliquot part of the drug taken.

Pill masses should always be made, according to the nature of the mass, either in iron or Wedgwood mortars, of the shape shown in Figs. 236 and 237, and the mixture should be frequently scraped from the pestle and the sides of the mortar with a stiff spatula so as to bring all particles repeatedly under the pestle. Trituration by means of a pestle is essential to produce a uniform mixture of the ingredients; and, moreover, it will be found that a mass can be formed in less time, with less excipient and less labor, in a mortar than on a pill tile. Very simple combinations, such as blue mass and extract of colocynth, etc., may be effected on the pill tile; but for all substances requiring uniform blending of fine powders, and similar cases, the use of the tile is to be condemned. Unfortunately, the





FIGS. 236 and 237.—Sectional view of properly shaped pill mortars.

misuse of the pill tile is a characteristic of many American pharmacists. One rule should be strictly observed in making every pill mass, namely: *Never use the spatula with which the mass is scraped down for taking excipient from its container.*

In manufacturing establishments large quantities of pill masses, which cannot be conveniently handled in a mortar, are made in special apparatus known as mass mixers, operated by either hand or steam power. Sometimes these kneading machines consist of smooth iron rollers (for white pill masses hard wood rollers are generally used) which revolve in opposite directions, some being so constructed that they can be warmed, if necessary, by passing steam through them. In all cases the ingredients for the mass are first roughly mixed in a basin or tank, and then repeatedly passed between the rollers until a uniform mixture has been produced. In Figs. 238 and 239 are shown other styles of mass mixers. Fig. 238 is a hand machine having a capacity of 3 pounds of mass, made by J. H. Day & Co., of Cincinnati, O.; the tank is porcelain-lined and the corrugated iron rollers or mixers

are galvanized, the finished mass being easily removed by tilting the machine and at the same time causing the rollers to revolve in a reverse direction. Fig. 239 represents a large power mixer made by the Arthur Colton Co., of Detroit, Mich., capable of handling 30 pounds and over of mass, sufficient for more than 100,000 two-grain pills.

Excipients.—It being impossible to select one single substance as an excipient suitable for all pill masses, owing to the variable properties of drugs and the many different combinations ordered by physicians, it is essential that the pharmacist be familiar with the peculiarities of each excipient, in order to use the same intelligently and advantageously. Excipients for pill masses may be divided into three distinct classes, as follows:

1. Those which are intended to develop adhesiveness, and hence act as solvents. To this class belong water, alcohol, diluted alcohol, glycerin, and a mixture of glycerin and water.

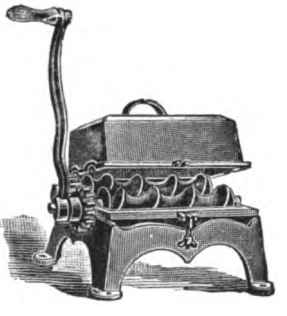


FIG. 238.—Hand machine for mixing pill masses.

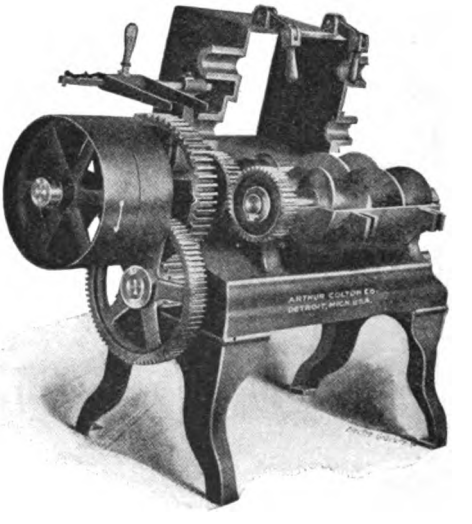


FIG. 239.—Mass mixer (open).

2. Those which are intended to impart adhesiveness; these may be fluid, semifluid, or solid. To this class belong syrup, glucose, honey, mucilage and syrup of acacia, mucilage of tragacanth, glycerite of starch, acacia with glucose or honey, tragacanth with glycerin, soap with water or diluted alcohol, extract of malt, confection of rose, manna and powdered elm bark mixed with tragacanth; the last named requires the addition of syrup or glycerin and water.

3. Those which are intended to act simply as absorbents of excessive moisture and, in a few cases, impart adhesiveness to the mass at the same time. To this class belong powdered licorice root, soap and licorice root, calcium phosphate, powdered orris root, powdered tragacanth, powdered elm bark, starch, and powdered marshmallow.

The first class, solvents, are employed in many cases in which physicians order vegetable powders in connection with soap or solid extracts, the latter in insufficient quantity to form a good mass. Solvents must be added to pill masses with great care, especially when water or glycerin is used with soap or extracts; by adding the fluid in drops and working the mass well after each addition, the required consistence will soon be developed, and a firm yet plastic mass be obtained, while an excess of moisture causes a softening of the mass, which frequently increases, and prevents the formation of perfect pills, besides requiring the addition of absorbent powders, which add to the bulk of the mass.

The second class, adhesive excipients, are more extensively used than any other, because the majority of substances prescribed in pill form do not possess inherent adhesive properties, or at least insufficiently, for properly massing the ingredients. Mucilage and syrup of acacia are the least desirable of the class, unless the pills are for immediate use, as pills made with acacia are prone in time to become very hard; the addition of glycerin, however, obviates the difficulty. Syrup or glucose is usually preferred to water for massing vegetable powders, in the absence of soap or solid extracts. Tragacanth with glycerin can be most conveniently used in the form of a jelly, made by triturating 85 grains of powdered tragacanth with 6 fluidrachms of glycerin and 1 fluidrachm of water; it is an excellent excipient for the salts of quinine, salol, acetanilid, sodium salicylate, iodoform, calcium sulphide, and also gallic and tannic acids; but for cinchonidine sulphate or salicylate, acacia with glucose or honey is preferable. Soap with water or diluted alcohol is the best excipient for aloes, rhubarb, and the various gum-resins; it cannot, however, be used with soluble metallic salts, as those of iron, lead, copper, etc., owing to the formation, by mutual decomposition of metallic oleates, which cause the mass to crumble.

The necessary precaution regarding the use of water in conjunction with soap has been mentioned above; an excess of the former invariably causes trouble. Manna is very desirable for massing reduced iron or manganese dioxide when these are prescribed alone. Extract of malt is very similar to glucose in its applicability, but can be used only for dark-colored masses. Confection of rose, at one time much esteemed as an excipient for mixtures of vegetable powders and metallic salts, has now gone out of use. For the valerianates of iron, quinine, or zinc, no better excipient can be used than acacia and alcohol in the following proportions: Iron, quinine, or zinc valerianate, 30 grains; powdered acacia, 10 grains; alcohol, 5 minims. Camphor and monobromated camphor can be made into very satisfactory pill masses by the addition of soap and oil of sweet almond or castor oil; about $2\frac{1}{2}$ grains of soap and 5 drops of oil will be sufficient for 30 grains of camphor.

As an excellent adhesive agent for heavy metallic salts, such as bismuth subnitrate or calomel, as well as for the scale salts of iron

and troublesome combinations like capsicum, camphor, and lead acetate, Mattison's excipient powder will be found very serviceable; it consists of 1 part of powdered tragacanth and 7 parts of finely powdered (No. 80) elm bark. Only a very small proportion of the powder is required, thus: 3 grains for 60 grains of bismuth subnitrate, calomel, cerium oxalate, iron by hydrogen, or equal parts of camphor and lead acetate; 6 grains of the powder for 60 grains of dried ferrous sulphate, the scale salts of iron, or equal parts of camphor and capsicum, etc. In all cases in which this excipient powder is employed, the mass should be made up rather soft with syrup, otherwise it is likely to crack or crumble while the pills are being formed; pills thus made become sufficiently firm and retain their original shape, on account of the fibrous and adhesive character of the excipient. Hager has recommended a similar powder, composed of 1 part of powdered marshmallow root, 1½ parts of powdered tragacanth, and 6 parts of powdered orris root; this powder can be used like the preceding, and is better adapted to white pill masses. In place of syrup, a mixture of 2 volumes of glycerin and 1 of distilled water may be used for pills which it is desired to keep soft.

At one time, crumb of bread was ordered quite frequently as an excipient for pill masses, particularly in cases in which it was intended at the same time to serve as a vehicle for the administration of potent remedies, as in the case of mercuric chloride, strychnine, etc. In place of bread crumb, which is not always available, either of the excipient powders mentioned above may be used, or a mixture of 1 part of tragacanth and 3 parts of starch, the mass to be made with glycerin and water, as before stated. The salts of quinine and cinchonidine are sometimes prescribed in pill form, in combination with aromatic or diluted sulphuric acid, the quantity of acid being often left to the judgment of the dispenser. As a rule from one-third to one-half as much acid as alkaloidal salt is sufficient to make a satisfactory mass, depending somewhat upon the condition of the atmosphere. The mass must be rolled out as soon as it becomes plastic, while still a little soft, otherwise it becomes dry and crumbly; in the latter case, the addition of a drop or two of syrup, or a very small quantity of glycerite of starch, restores the proper condition. Quinine sulphate triturated with one-sixteenth of its weight of tartaric acid becomes damp and adhesive, and upon the further addition of a small quantity of glycerin (about 15 or 16 drops to 100 grains of quinine sulphate) yields an excellent mass, the pills being small and firm. If kept in a cool, dry place, such pills retain their original condition for a long time; but if carelessly preserved, they absorb moisture and become soft, and are apt to stick together. Although strong mineral acids are rarely prescribed in pills, they are occasionally used, in combination with pepsin and vegetable powders, in prescriptions written in Germany; the excipient powder mentioned in the preceding paragraph together with glycerin and water, will yield a good mass.

Easily reducible substances, like silver nitrate, potassium permanganate, silver oxide, gold chloride, etc., cannot be massed with the usual excipients, as they need some adhesive agent which will not cause decomposition. The most available substances are white clay (kaolin) and water, which form a plastic mass, but one requiring quick manipulation, as it soon becomes dry and crumbly. The following excipient, proposed by M. Carles for pill masses of this character, namely, a mixture of 2 parts of kaolin and 1 part each of anhydrous sodium sulphate and water, has proved satisfactory. Sixty grains of kaolin and 30 grains of the sodium sulphate require 40 minims of water to form a plastic mass, which dries slowly and retains its plasticity for six or eight minutes; it admits of much better manipulation than do clay and water alone, and the pills, when formed, soon become hard and retain their shape, owing to the assumption of the crystallized state by the anhydrous sodium sulphate under the influence of water. When potassium permanganate is to be made into pills with this excipient, a larger quantity of water must be used; the best plan is to rub 30 grains of potassium permanganate into fine powder, mix well with 30 grains of kaolin and 15 grains of anhydrous sodium sulphate, and then mass with sufficient water, usually 25 to 30 minims. A mixture of equal parts of kaolin, or fuller's earth, soft petrolatum, and paraffin, forms a most excellent excipient for this class of pills; or the medicinal agent, in fine powder, may be incorporated with its own weight of lanolin, or wool fat, deprived of its water, and then sufficient kaolin be added to form a mass. Lanolin is indifferent toward silver nitrate and potassium permanganate (Hager). Another satisfactory method is to mix potassium permanganate with one-half or the whole of its weight of kaolin, and then mass with one-fourth its weight of soft petrolatum.

When deliquescent substances, or such as slowly volatilize upon exposure to air, are ordered in pill form, a mixture of potassium borotartrate with half its weight of water will prove a good excipient; about $\frac{1}{6}$ of a grain of powdered tragacanth should be added for each pill, and the mass must be quickly formed and rolled out; 60 grains of hydrated chloral or 30 grains of potassium iodide require 2 drops of the excipient. Even potassium acetate has been made into satisfactory pills by the aid of potassium borotartrate, 18 parts of the former and 3 parts of the latter being used with 1 part of water. All such pills should be dispensed in bottles.

The third class, absorbent excipients, are frequently required to supply the necessary firmness to a pill mass, so that the original shape given to the pills may be retained. The addition of absorbent powders must be made judiciously, so as to avoid an unnecessary increase in the bulk of the mass, and the quantity used should be noted on the prescription, so that in case of a repetition pills of the same size may be dispensed. The reckless use of solvent as well as absorbent excipients is one of the chief errors of inexperience, and

often causes much trouble. Some absorbent powders, such as starch, calcium phosphate, magnesium carbonate, licorice root, and orris root, possess little or no adhesive properties, and if used in excess will cause the mass to crumble; others, like marshmallow root, acacia, and elm bark, containing much mucilaginous matter, if used in excess, form hard and slowly soluble combinations.

For pill masses containing an excessive quantity of soft, solid extracts, powdered licorice root will be found very desirable and preferable to powdered elm bark, unless metallic salts are present in large proportion. For volatile oils, creosote, and liquid oleoresins, soap is decidedly the best excipient, as it emulsionizes these and prevents their separation during subsequent manipulations; from ½ to 1 grain of soap is necessary for each minim of oil, and stearin or curd soap will be found preferable to olive oil soap. In the absence of any vegetable powder in the prescribed combination, the addition of powdered licorice root is desirable, and a mixture of 1 part of soap and 5 parts of licorice root forms a convenient excipient, of which 3 grains should be used for each minimum of volatile oil; if necessary, water or diluted alcohol may be used to facilitate massing. The incompatibility of soap and soluble metallic salts in pill masses has been noted in a previous paragraph. For creosote, when ordered by itself, powdered licorice root and water are very serviceable; 2 grains of the powder with a little water are sufficient for each drop of creosote. Phenol (carbolic acid) can be treated like creosote, and soap will be found to bind it very nicely.

Tar, when prescribed in pill form, either alone or in connection with other remedial agents, requires the addition of an absorbent; magnesium carbonate and powdered licorice root have been recommended, but calcium phosphate, used in twice the weight of the tar, has been found more satisfactory, yielding a firm yet plastic mass. Pills thus made retain their original shape and disintegrate readily in water. For making pills of mercurial ointment the same excipient has been used with success.

Hager has suggested a mixture of equal weights of yellow wax and starch, in the form of powder, as a superior adhesive and absorbent excipient for numerous troublesome pill masses; starched wax is decidedly preferable, as an excipient, to wax with an addition of some fibrous vegetable powder, as pills made with the former disintegrate more rapidly, and the wax, being in a state of fine division, is less liable to cause intestinal trouble. From 3 to 5 grains of starched wax will yield a satisfactory mass with 1 grain of each of the following substances (Hager): carbolic acid, apiol, oleorsin of male fern, guaiacol, creosote, croton oil, terpinol, and oil of tar. Starched wax may be prepared by thoroughly drying yellow wax, in the form of thin shavings, under a paper cover in a dark place, and then rubbing into powder with an equal weight of rice flour.

Unless some other substance is present, as an oleoresin or a volatile

oil, whereby the melting point of the mixture is brought down to about 38° C. (100.4° F.), wax is very undesirable in pill masses on account of its difficult disintegration, which may cause pills made therewith to pass through the body unaltered. When wax is directed to be used in a pill mass, it should be melted at a moderate heat and then mixed with any oil or oleoresin ordered, before the solid ingredients are added.

Powdered tragacanth may sometimes be employed as an absorbent when it is desired to impart adhesiveness to a very moist mass without materially increasing the bulk. The mixture of tragacanth and powdered elm bark, previously mentioned, is, however, generally to be preferred. The compound tragacanth powder of the British Pharmacopœia, composed of 1½ parts of powdered tragacanth, 2 parts each, powdered acacia and starch, and 4½ parts of powdered sugar, forms an excellent absorbent and adhesive agent.

A mixture of equal parts of finely powdered elm bark and starch will be found a most desirable excipient for soft pill masses containing iodine or iodide of iron; the mass should be rolled out while still moderately soft, as the pills will harden subsequently. Pill masses containing free iodine should invariably be made with the addition of starch, which, combining with the iodine, prevents its irritating effect on the mouth and throat; the union between the starch and iodine is very feeble, and the latter will be liberated by the warm liquids of the stomach.

In a few cases the addition of any excipient is superfluous, as when lupulin and camphor are ordered together in pill form. The simple trituration of powdered camphor with lupulin causes the resinous matter to soften, and an adhesive mass is quickly obtained which hardens on standing. All solvents, like ether, alcohol, and diluted alcohol, must be avoided, but a very small quantity of elm bark may sometimes be added with advantage in very warm weather.

Mortars and other utensils used in making pill masses are sometimes cleaned with great difficulty, on account of the stain imparted by certain chemicals. As a rule plain water, cold or hot, will suffice to remove the slight remnants of a pill mass, especially if allowed to stand in the mortar for a short while; but in some cases the addition of lye (caustic potassa or soda solution) becomes necessary to soften hard resinous deposits. The persistent odor of volatile oils is best removed with a little alcohol after the mortar has been well washed with water. A few drops of oil of turpentine promptly remove the odor of iodoform. Metallic stains, as a rule, are dissolved quickly by a little strong hydrochloric or nitric acid. Manganese dioxide stains disappear at once if treated with coarsely powdered ferrous sulphate, sulphuric acid, and water; while potassium permanganate stains yield readily to a solution of oxalic acid.

Division of the Pill Mass.—After the mass has been properly prepared, it is transferred to a pill machine or a graduated glass or porcelain tile,

to be rolled out, by means of a flat piece of hard wood, into a rod or pipe of uniform thickness, which is then divided into the requisite number of pieces. Steel spatulas are used by many for rolling out the mass, but are not so desirable as a wooden roller, since the width of the spatula permits of covering only a small part of the mass at a time, hence irregularity in the thickness of the cylinder frequently occurs. A little pressure must be applied when rolling out the mass, both on the

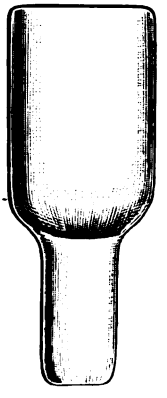


FIG. 240.—Wooden pill roller.

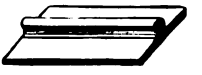


FIG. 241.—Pill roller.

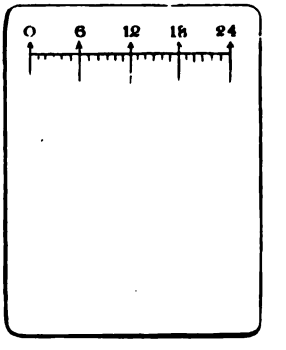


FIG. 242.—Pill tile, graduated.

pill machine and tile. Figs. 240 and 241 represent wooden pill mass rollers, the long one with the handle having the more convenient shape.

A small number of pills may be conveniently divided on a pill tile (Fig. 242), but for a larger number a pill machine will be found preferable, particularly if the weight of the pills corresponds to the size of the grooves, for then the perfect rounding of the pills can be readily effected by continued rolling in these grooves. In order to insure greater uniformity in cutting the mass on a pill tile into

FIG. 243.—Livingston pill cutter.

the requires number of parts, use may be made of either of the two devices shown in Figs. 243 and 244. The Livingston pill cutter may be used to cut 24 parts at one time by simply pressing the steel cutters into the pill mass after the same has been rolled out to the required length by means of a wooden pill paddle; the separate pieces may then be quickly ejected by means of a slotted metallic strip operated by a spring on the top of the bar. The Diamond pill cutter is combined with a flat wooden roller for rolling the mass

out to the required length, which is then brought under the projecting cross-piece and the metal cutters pressed down upon it; as the metal plate, to which the cutters are attached, rebounds to its original position, the latter are stripped of any adhering pieces of mass by the projecting cross-piece, through the slots of which the cutters pass. Fig. 245 represents a complete pill machine. It consists of a smooth, hard wood rolling-board encased in metal and provided with a grooved

FIG. 244.—Diamond pill cutter.

metal plate; to the roller, which is likewise made of hard wood is attached a similar metal plate, the grooves of which correspond exactly to the grooves of the plate on the board, being adjusted to the size of pills of certain weights, as 1, 2, 3, or 5 grains. To facilitate the motion of the roller, it is frequently provided with two little metal wheels on each side of the grooved plate, as may be seen in the illustration. When the roller is in use, these bear against the metal casing of the rolling-board and thus enable the roller to travel uniformly.

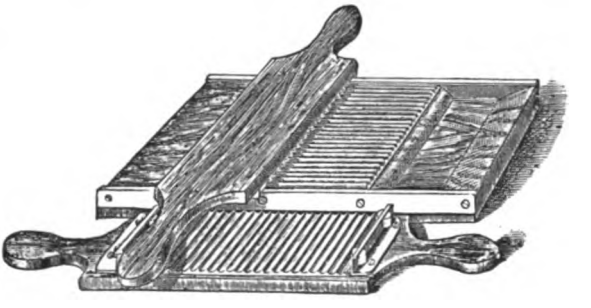


FIG. 245.

The best pill machine is the "Cooper patent" (Fig. 246), the woodwork being of mahogany and the metallic parts of brass. This machine has two sets of reversible grooved plates, on which four different sizes of pills can be made—1, 2, 3, and 5 grains; the plates being quickly removable and adjustable. The sides of the rolling-board are so constructed that they can be raised or lowered by means of winged screws, which allows the mass to be rolled just the thickness required for each respective size of pill, thereby insuring always the full number of perfectly round pills.

After the mass has been properly rolled out to the length of the desired number of pills, it is laid upon the grooved plate of the board, and divided by placing the other cutter over it and drawing the same forward and backward with slight pressure.

When the pill mass has been divided on a pill tile, and also when the pills are larger or smaller than the grooves of the machine, it becomes necessary to impart a spherical shape to the pieces, by

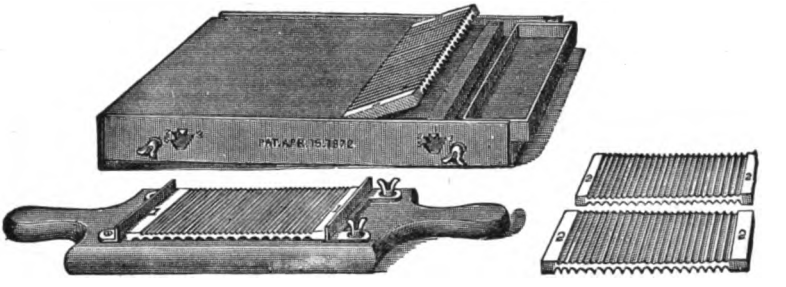


Fig. 246.—Cooper's patent pill machine.

appropriate rolling between the thumb and the index and middle fingers, after which the pills should be placed under a pill finisher and completely rounded by rotary motion of the same with some pressure. It is better to move the finisher about in curvilinear figures like the figure 8, instead of giving it a constant circular motion, so that the pressure may be uniform at all points. Pill finishers usually consist of a circular piece of hard wood, with a smooth rolling surface and a projecting margin for the purpose of confining the pills; several sizes are required to suit different sizes of pills. Fig. 247 represents a convenient pill finisher suitable for two different sizes, as the upper and lower margins project to different lengths.

Fig. 247.—Hard wood pill finisher.

Pill Dusting.—The pill mass, being plastic and adhesive, is prone to adhere to the slab and the fingers while being rolled out and shaped into pills. This may be prevented by the use of a fine powder, which should be wholly inert, unless otherwise directed by the physician. Among the most suitable powders are lycopodium, licorice root, and starch. The former is particularly desirable on account of its fineness and uniformity, its slight adhesiveness, and its tastelessness. Powdered starch should be used with all white pill masses, Bermuda arrow-root being the best for the purpose. Only in exceptional cases is the addition of dusting powder to the pills in the box justifiable; the pills should receive a sufficient coating of the powder under the finisher; then, if the mass has been properly made, there will be no likelihood of the pills adhering, hence no occasion for putting an excess of powder

in the box. Magnesia and magnesium carbonate are not well suited for dusting powders, and should, moreover, be used with due care, on account of the possible chemical effect upon the ingredients of the pills. Powdered talc (soapstone) is likewise serviceable, having the advantage of imparting a very thin, opaque, and tasteless coating to the pills, without impairing their solubility in the stomach; it is particularly suited for pills of silver nitrate and the like. When asafetida or other nauseous substances are given in the form of pill, the odor may be either entirely disguised or considerably modified by the use of powdered cinnamon, aromatic powder, ginger, or similar material.

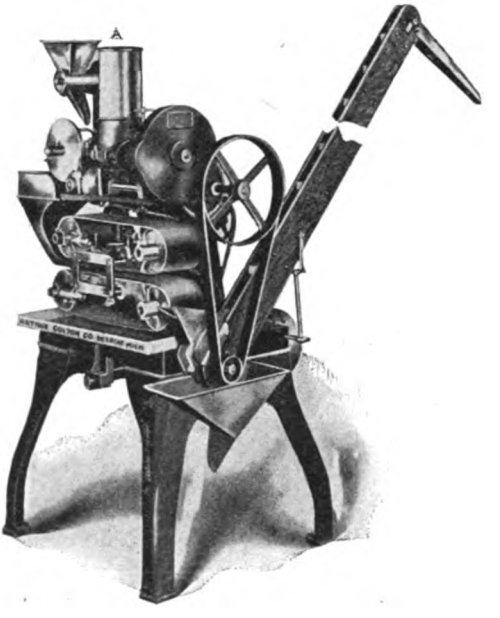


FIG. 248.—Ball making machine.

The manufacture of pills on a large scale has reached enormous proportions, and of late years automatic machines have been designed having a daily capacity of from 250,000 to 1,000,000 pills. Anyone unfamiliar with recent developments and improvements in apparatus and machinery used in the large manufacturing houses of this country can form no idea of the extent and perfection of the work. After the mass has been completed it is fed into a ball making machine, and is then not again handled until the finished pills, either round or oval, are deposited in the receiving trays. In Fig. 248 is shown one of a series of ball making machines made by the Arthur Colton Co., of Detroit, Mich., capable of producing from 10 to 60 balls per minute. It is operated as follows: The crude mass taken from the mass mixer is placed into the hopper *A* and is at once rolled and pressed forward

to a point where a piece is automatically cut from the mouth of the nozzle by a special device capable of producing any size desired. The piece cut loose from the roll of mass then falls into a guide receiver, where it is dusted and allowed to drop through another guide to be deposited in the centre of the rolling belt made of rubber; it finally falls to a natural position at the base of the elevator, where it is gently lifted to the top of the conveyor, to be dropped into the receiving funnel attached to the automatic pill machine, one of which is shown in Fig. 249.

As each ball is delivered to the piping belts of the latter machine it is rapidly advanced and becomes elongated into a pipe from the fact of being rolled hundreds of times about its own diameter with

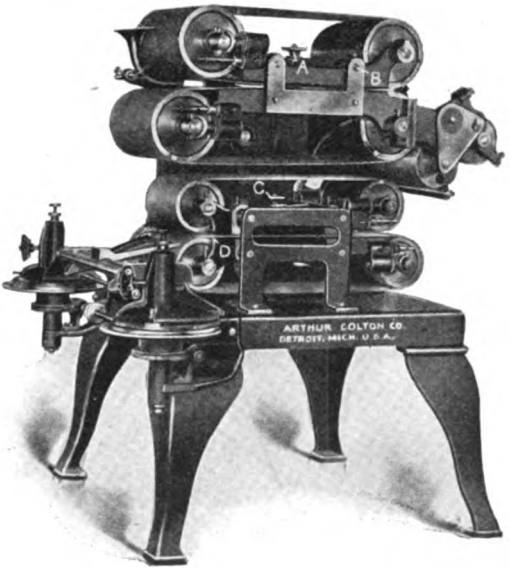


FIG. 249.—Automatic pill machine.

gentle pressure given as it advances between the belts. When the pipes are finished they drop onto revolving cutters to be instantly divided into pieces of accurate weight and shape; these pieces drop onto a chute which conveys them to the entrance of the rounding belts, where they are thoroughly rolled and sent forward to the receiver or separator. Perfect spherical shape is imparted to the pills by this latter treatment, and if oval pills are desired, they are conveyed by means of a chute to the shapers, where the elongation is quickly effected.

The precise automatic work of these large pill plants is marvelous, and reflects great credit on the designers and makers of the machines, which are now in use in nearly all the large pharmaceutical manufacturing houses.

Pill Coating.—The plan of coating pills with various substances with a view to mask the odor and taste of nauseous medicines, is by, no means a novelty, having been practised more than fifty years ago. At one time the silvering or gilding of pills was of frequent occurrence, but at present it is but rarely employed. Pills to be thus coated must be made firm and rolled perfectly smooth, if possible without any dusting powder; they should be very slightly dampened with a mixture of equal parts of alcohol, syrup, and mucilage of acacia and then placed in a suitable apparatus consisting of two hollow hemispheres of hard wood or horn, as shown in Fig. 250. Silver or gold foil is added, when, the apparatus having been closed, a rapid rotary motion will in a very short time cause the pills to take on a uniform coating of the metal; should some of the pills receive only a partial covering, more foil must be added and the rotary motion repeated. As a rule one leaf of silver or gold will cover a half-dozen 3-grain pills. Glycerin should not be used as an excipient for pills which are to be silver- or gold-coated, as it will lessen the brightness of the metal.

FIG. 250.

Sugar coating is a process which is not readily applicable to the operations of the pharmacist, requiring experience and practice to insure success. It partakes of the confectioner's art, although the coating of pills with sugar requires somewhat more care, on account of the absence of starch or flour, which generally make up a part of the confectioner's coating. Sugar coating of pills on a large scale is done in hemispherical copper pans made to revolve slowly within a coil of steam pipe supplying the necessary heat for evaporation of the moisture; the pills, which should be well air-dried, are placed in the pan, and a quantity of simple syrup or of a mixture of syrup and mucilage of acacia is poured on, the pan being kept in constant rotary motion until the pills are dry. The addition of syrup is repeated until a sufficiently thick coating has been deposited in the pills, and this can be determined only by experience.

Sugar coating can be more successfully performed with a large quantity of pills than with a small number, as the deposit of sugar takes place more uniformly, and the mutual attrition of many pills insures a smooth surface. Fig. 251 represents a sugar coating pan in use in large manufacturing establishments; as seen in the illustration, it is operated entirely by steam power. For small operations it will be found desirable to dampen the pills with diluted mucilage of acacia or egg albumen and then rotate them in a tinned copper or a porcelain dish containing either finely bolted sugar or a mixture of acacia 1 part and sugar 5 parts, or of sugar 2 parts, sugar of milk

1 part, and purified talcum 1 part. With care and practice very fair results may be obtained, although the pills should not be expected to look so perfect as those coated by machinery. A small apparatus

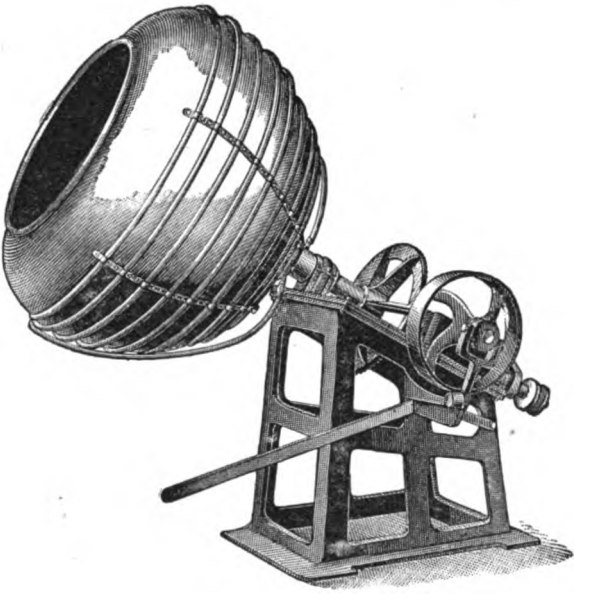


FIG. 251.—Sugar coating machine for pills.

has been devised in England for facilitating the sugar coating of pills at the dispensing counter; it is shown in Fig. 252, and consists of a flat-bottomed, tinned copper pan, with a hinged cover. The pills

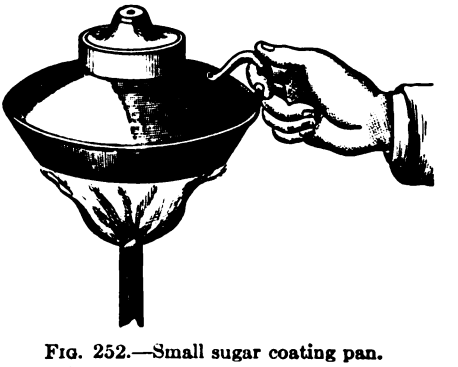


FIG. 252.—Small sugar coating pan.

having been dampened as directed, may be placed in the pan with the sugar and rotated while a gentle heat is applied, which facilitates the drying of the coating; when dry, the process can be repeated until

a perfect, hard, white coating is obtained. Sugar-coated pills do not at first have the familiar glossy appearance, but are dull when taken from the coater; a suitable polish may be given the coated pills by rotating them in a drum having a canvas body coated with paraffin (see Fig. 253), whereby a minute film of paraffin is deposited on the sugar coating and thus the desired gloss produced; for small quantities of coated pills, these may be shaken in a muslin bag with small pieces of paraffin, whereby a similar gloss is obtained. The same treatment may be applied to chocolate-coated pills or tablets, which likewise lack a glossy finish when first made.

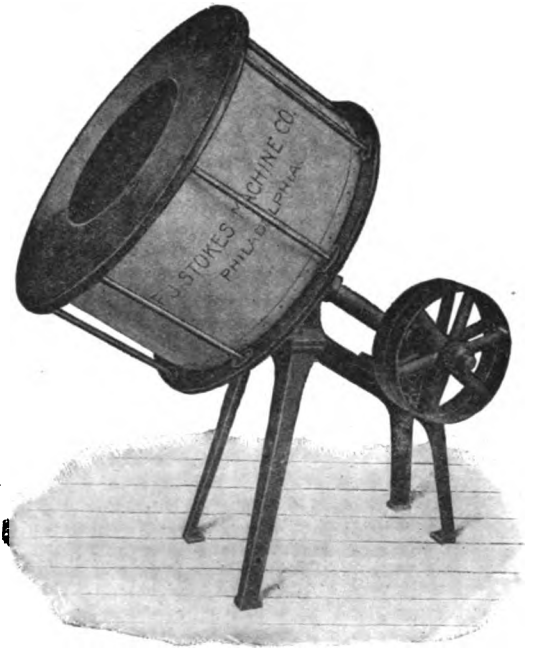


FIG. 253.—Polishing machine.

Gelatin coating is more readily applied than sugar coating, but, like the latter, requires practice to insure proficiency. The chief difficulty lies in the drying of the coating after the pills have been dipped into the solution of gelatin; the pills must be kept in motion while the gelatin cools, otherwise the coating will not be uniform. Pills to be gelatin-coated must be firm, dry, and free from dusting powder; if glycerin is used as an excipient, it is likely to soften the gelatin coating, causing the pills to stick together. For pills containing strongly odorous substances, such as asafetida, sumbul, iodoform, the valerianates, etc., gelatin coating is decidedly inferior to sugar coating, as the odor penetrates gelatin far more rapidly than sugar. The manner of coating the pills on a large scale is identical with that

used for only a dozen pills, namely, the pills are impaled upon long, thin needles, to the depth of about $\frac{1}{16}$ of an inch, and then immersed in a solution of gelatin kept fluid by means of a waterbath; in order to avoid contraction and cracking of the gelatin upon cooling, mucilage of acacia is usually added to the solution, and, by some, syrup also. The rapid drying on a large scale is effected by placing the pills soon after they have been dipped, while still on the needles, in specially constructed drying cases connected with an exhaust fan, by means of which air is rapidly drawn through the cases, and the moisture is thus removed.

For small operations various devices have been suggested for drying the gelatin coating, no one of which can be said to be the best, as pharmacists prefer that apparatus with which they have become most familiar by practice. The gelatin solution should be kept at a temperature of between 72° and 82° C. (161.6° and 179.6° F.), so that it may not be too thick when the pills are immersed, and any scum or froth forming should be carefully pushed aside before the pills are dipped. Figs. 251, 252, and 253 represent the three leading styles of gelatin coating apparatus in use among pharmacists in this country. In two of them the pills are taken up on the needles from a tray provided with grooves, in which the pills have been placed, and, after they have been dipped into the gelatin solution, are revolved until dry and then stripped from the needles by means of a comb, shown in the illustrations. The gelatin solution recommended by Prof. Patch has been found very useful; it is made as follows: Macerate $2\frac{1}{2}$ ounces (av.) of French gelatin (gold label) with 7 fluidounces of distilled water, and when soft, dissolve by aid of a hot waterbath; add 2 drachms of boric acid, and finally 2 fluidounces of mucilage of acacia; strain the mixture.

The "Porcupine" gelatin coater (Fig. 254), designed by C. C Wells, consists of a wooden tray, *A*, provided with grooves and a gauge for regularing the depth to which the needles shall enter pills of different sizes, and also a brass comb for disengaging the pills from the needles; a drying cylinder, *B*, provided with T-shaped rails on its rounded cylinder, which form grooves for receiving the needle-bars, *C;* a waterbath and solution-holder, *D*, the latter being a trough in the cover of the bath and kept at the proper temperature by the aid of heat. After the needle-bars carrying pills have been placed in the grooves of the cylinder the latter is kept revolving, by means of the crank on the side (larger machines are operated by clock-work attachments), at the rate of about 50 revolutions a minute, until the pills are dry enough to stick together when taken off the needles. Wells recommends the following solution for gelatin coating: Disssolve 2 drachms of acacia in 1 fluidounce of water, and add 1 ounce (av.) of Cox's gelatin, 2 fluidounces of water, and 1 fluidounce of simple syrup; dissolve by heat and strain.

The gelatin coater of W. C. Franciscus (Fig. 255) resembles the

other two, except in the provision for drying the coating on the pills, which must be done by rapidly twirling the needle-bars centred on a

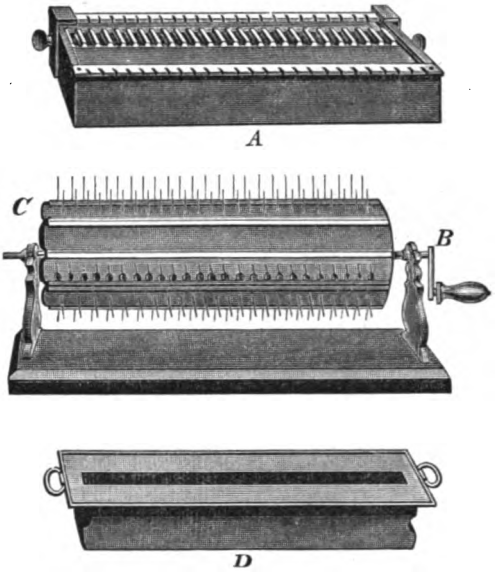


FIG. 254.—Wells' "Porcupine" gelatin-coater.

pivot with the hand, until the pills are sufficiently dry to be removed. The different steps of the operation are shown in the illustration: *A* represents a waterbath, and *C* the solution-holder resting in the same; *BB* shows the position of the needle-bar in the act of impaling

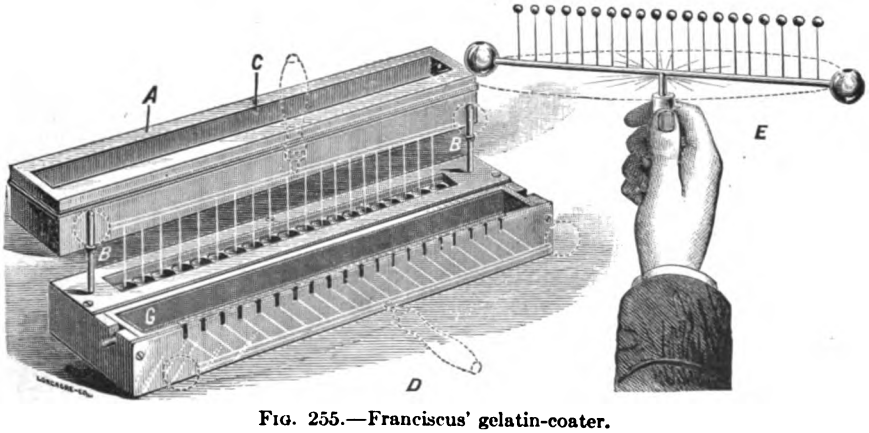


FIG. 255.—Franciscus' gelatin-coater.

the pills which have been placed in the depressions in the tray, the balls on the ends of the bar insuring accuracy in centring the pills

with the needle-points, by slipping over the rods *B* and *B*. At *E* is shown the manner of revolving the pills, after they have been dipped, by means of the pivotal handle *D*. When sufficiently dry, the pills are stripped from the needles by means of the comb attached to the tray *G*.

Maynard's gelatin coater (Fig. 256) is not provided with a grooved tray from which the pills are taken up, but, instead, the pills are placed in depressions in a metallic plate, *E*, provided also with two holes to receive the guide-pins attached to the circular needle-holder *D*, and surrounded with a metallic ring, *F*, to prevent the pills rolling off. When the needle-holder is not in use, the needle-points are drawn back behind the outer disk by means of the handle attached to the top, to which the needles are fastened. To impale the pills, the needles are depressed, passing through the perforations in the outer disk, and take up the pills as shown at *C*. The gelatin solution is

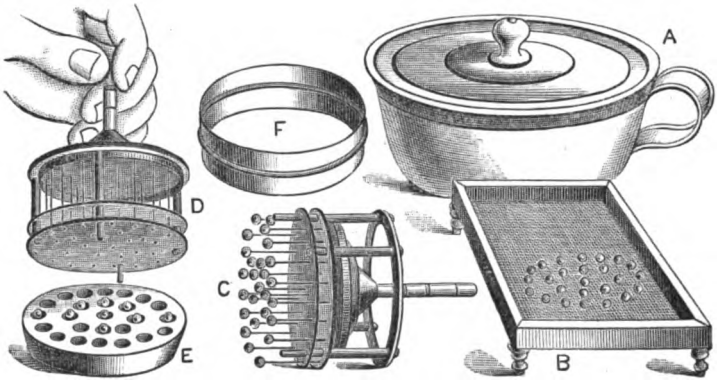


FIG. 256.—Maynard's gelatin-coater.

contained in a covered agateware dish, resting in the copper water-bath *A;* after the pills have been dipped, the needle-holder is slowly revolved to facilitate the uniform distribution of the gelatin film. When the gelatin has set, the needle-holder may be laid aside, as shown at *C*, until the coating is sufficiently hard to allow the pills to be removed to the tray of wire gauze *B*, by grasping the circular plate on the needle-holder with one hand and pulling the handle upward with the other. It is always well to grease slightly with petroleum the perforated disk, through which the needles pass, to prevent the pills adhering.

The application of a continuous coating of gelatin to pills without the use of needles, invented by J. B. Russell, is in successful operation at several large manufacturing establishments, but is not available at the dispensing counter, since extensive steam-power machinery is necessary for the work. In Fig. 257 is shown a modern machine

for gelatin coating pills, which requires but one operator, and has a capacity of 80,000 pills per day of ten hours. It is made by the Arthur Colton Co., of Detroit, Mich., and is provided with a rotary vacuum pump and an exhaust tank placed between the pump and machine for the purpose of obtaining a steady current without pulsation. The gelatin coating is applied as follows: The pills having been properly seasoned are stored in a drawer attached to the machine and provided with a feeding plate which registers with the dipping plate; the latter is placed on the vacuum jacket and clamped in place, after which the pill drawer is pulled forward, bringing the feeding plate exactly in proximity with the dipping plate. The vacuum

FIG. 257.—Gelatin pill coating machine.

having been applied, the pills are carefully brushed upon the feeding plate, when every receptacle will be filled, the pills being held in place by force of the suction supplied from the exhaust tank. The pill drawer is returned to its place, and the vacuum jacket containing the dipping plate and pills is now reversed for immersion. The coating having been applied, the jacket is inverted to its original position and the vacuum shut off. The plate is then released from its place and put into the kiln for the purpose of drying the pills by a current of warm air. The operation is then repeated with another dipping plate and another lot of pills, as previously described. The pills having become dry in the kiln, the plate is securely placed upon the transferring apparatus, and by means of a lever brought into close contact,

one above the other, with the dipping plate on the vacuum jacket, when by force of the vacuum acting through the perforations, the pills will be immediately released and transferred to the dipping plate. The operator then proceeds to immerse the uncoated half of the pills in the same manner as above described.

In place of gelatin coating at the dispensing counter, the plan prevails in this country of disguising the disagreeable odor and taste of pills by enclosing them in gelatin capsules. These gelatin capsules are sold under the name of *empty capsules*, and consist of small cylinders closed at one end and provided with a shorter cylindrical cover; they occur in seven sizes, ranging from $\frac{3}{8}$ inch to 1 inch in length, and are numbered respectively from No. 5 to No. 00; they are sold at fabulously low prices. The composition of the empty capsules made in this country is a mixture of gelatin and glycerin in variable proportions, dependent upon the character of the gelatin. The French Pharma-

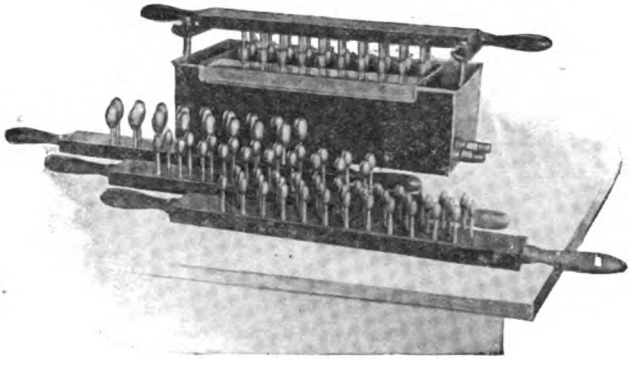


FIG. 258.—Stokes' gelatin capsule apparatus.

copœia recommends a mixture of 25 parts of white gelatin, 8 parts of white sugar, 10 parts of glycerin, and 45 parts of distilled water, to be dissolved on a waterbath. Other authorities propose for hard capsules a mixture of 60 parts of gelatin, 10 parts each of acacia and sugar, and 50 parts of water; and for soft capsules a mixture of 50 parts of gelatin, 16 parts of sugar, 20 parts of glycerin, and 90 parts of water.

The capsules are made by dipping either metallic, bone, or wooden moulds, attached by means of handles to a suitable disk or block, as shown in Fig. 258, into the melted gelatin mass kept at a temperature of about 40° C. (104° F.), and then rotating the moulds gently for a few minutes so as to insure a uniform film; if necessary, the immersion is repeated. To prevent adhesion of the gelatin solution to the moulds, the latter are rubbed with a soft oiled cloth before dipping them. After twenty to thirty minutes the gelatin film will have become sufficiently firm to allow the caspules to be stripped from the mould,

and laid aside to dry in suitable closets provided with a draft of moderately warm air, any excess of gelatin being removed with an ivory knife before the capsule is taken from the mould.

As the object of capsuling pill masses is to render the medicine as palatable as possible, care should be taken that the exterior of the capsule be not contaminated in any way with the material. This is best accomplished by dividing the mass into small cylindrical pieces, rounding off the ends of each, and then, after having washed the hands thoroughly, introducing the pieces, by the aid of a long needle, into the capsule held in the left hand, taking up the cover with two fingers of the right hand holding the needle and quickly slipping it into position, thus avoiding all contact of the mass with the exterior of the capsule. The habit of putting pills into capsules with the fingers is censurable and an evidence of bad training.

The filling of capsules with liquids is, as a rule, done in large manufacturing establishments, although the operation is easily within the reach of the pharmacist when small quantities are involved. For this purpose soft capsules of ovoid shape, with elongated ends or necks, are supported on trays or racks and the liquid is introduced by means of a pipette or a syringe with a small nozzle, care being necessary to avoid getting some of the liquid on the outside. The elongated ends are cut off just before the soft capsules are filled, and are placed in a small dish to be melted on a waterbath, the melted gelatin being subsequently applied with a warm glass rod to the orifice or open end of the capsules for the purpose of sealing them.

When soft capsules are not available, it is sometimes necessary to use the ordinary empty capsules for liquids. This is done in a manner somewhat similar to that directed above for soft capsules by setting the lower part of the capsules up in a suitable rack or a perforated box lid, and having introduced the liquid, the cap or upper part of the capsule with its edges moistened in a drop of water spread on a pill tile or by pressing against a piece of wetted filter paper, is slipped over the lower part with a little pressure, and the capsule thus hermetically sealed.

Liquids containing water, or others likely to affect the gelatin-glycerin body of capsules, cannot be dispensed in capsules; thus, creosote, being soluble in glycerin, should be mixed with 2 or 3 times its volume of expressed oil of almond before it is introduced. Sometimes, when the ordinary empty capsules must be used, it may be advisable to mix the liquid to be dispensed in capsules, with starch or finely powdered licorice powder and make a firm paste with a few drops of water or syrup, which can then be formed into small rod-shaped pieces and placed in the capsules in the manner directed above for pills.

The well known globules or pearls of oil of sandalwood, oleoresin of cubeb, apiol, chloroform, etc., are elastic capsules filled with the respective liquids. They occur in both oval and round shape of

varying capacities from 3 to 80 minims. The first step in their manufacture is the making of the gelatin leaves or sheets, which is done by allowing a solution of gelatin in glycerin, while still warm, to flow onto square steel plates which are either covered with amalgam or tinned, so as to insure a perfectly smooth surface. For this purpose the apparatus shown in Fig. 259 is used, the gelatin solution being allowed to flow from the copper tank by means of a faucet onto the plates held in position on the table by means of grooves, the thickness

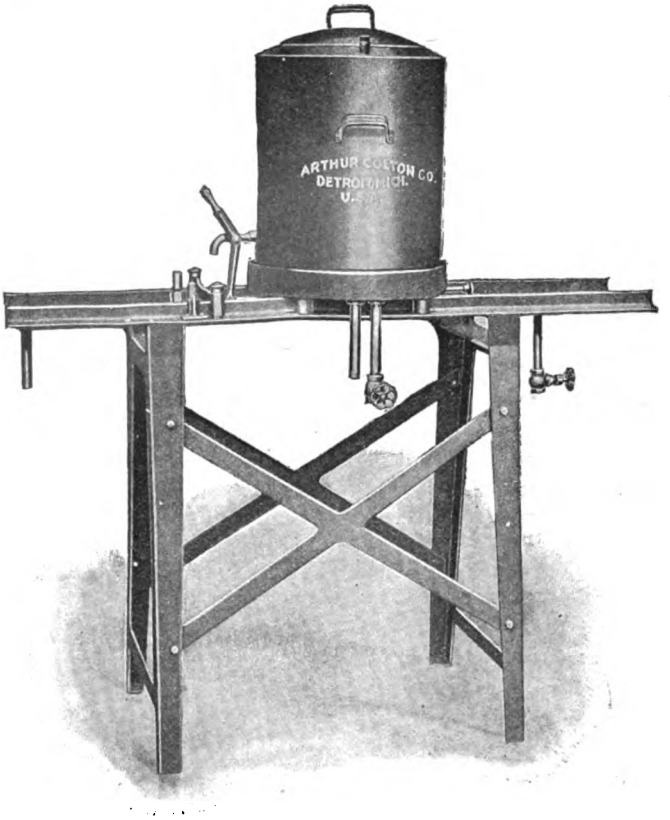


FIG. 259.—Gelatin leaf or sheet machine.

of the leaves being regulated by use of an adjustable gauge; the plates thus covered are then transferred to racks in suitable drying closets, where the gelatin sheets are allowed to dry during 24 hours.

To make the globules or pearls, a gelatin leaf is placed on a mould specially constructed for that purpose, consisting of compact bronze plates with numerous perforations, from 38 to 368, according to the size of the globules intended, into each of which is inserted a hard steel tube, as shown in Fig. 260. The lower mould *B*, having been

fitted into the frame *A* and previously slightly heated on a warming table, is entirely covered by the gelatin leaf, which soon conforms itself to the various corners and ledges in the frame. A measured quantity of the liquid to fill the globules is now poured on the leaf, and another leaf is then placed over the liquid in such a manner as to exclude all air; this operation requires some little care, but skill is soon acquired by practice. After placing the upper mould *C* exactly over the lower with the aid of guide pins the whole is transferred to a powerful press. The moulds having been placed in position, the table of the press rises slowly and perfect sealing of the gelatin leaves is effected by powerful pressure of from 3 to 5 tons, the gelatin being cut clean by the edges of the steel tubes. Upon release of the pressure, the table recedes and the moulds are removed and opened, when the individual globules or pearls can be easily obtained by stretching the leaf from opposite corners. They are finally cleaned by means of a suitable solvent to remove any excess of liquid adhering to the exterior.

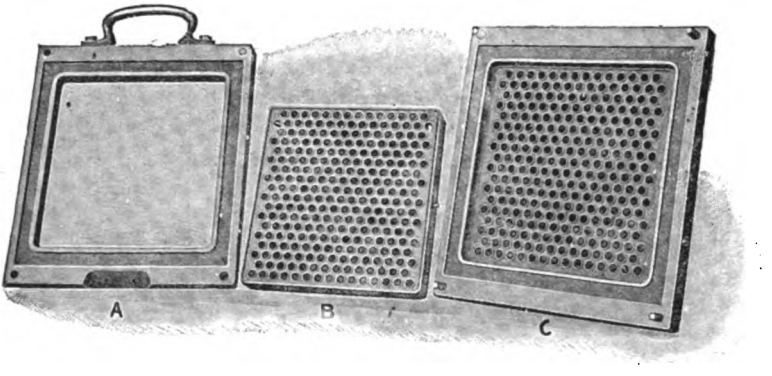


FIG. 260.—Pearl or globule mould.

Another method is said to consist in filling a tube, made of gelatin composition, with the respective liquids, and then, by means of a specially constructed machine, cutting off pieces of the required size and simultaneously pressing these into the proper shape. The apparatus used for this method is known as Viel's capsulator.

Pills are sometimes coated with collodion or balsam of tolu, the latter plan being directed in the official formulas for pills of iodide of iron and of phosphorus. To coat pills with collodion, they are simply impaled on needles and dipped into collodion, which is then allowed to dry; if water be present in the pills, the coating will become mottled or opaque. The Pharmacopœia directs a solution of 10 Gms. of balsam of tolu in 15 mils. (or Cc.) of ether, for coating pills, but, owing to the very rapid evaporation of the solvent, the process is unsatisfactory, as the pills are prone to stick. The following improvement by Dunning has met with considerable success: Dissolve 5 Gms.

of balsam of tolu in 15 mils. (or Cc.) of alcohol with aid of a gentle heat; strain, and when cold add 5 mils. (or Cc.) of ether. Enough of this solution is poured into the lid of an 8-ounce ointment jar to form a thin layer, the pills are added, and the lid rotated until they are completely coated. The pills are then transferred to another lid, previously coated with liquid petrolatum by spreading one drop over the surface with the finger, and rotated for a few minutes to remove the excess of the tolu solution. They are finally placed in a third lid, coated like the second, and rotated until dry.

The so-called "pearl coating" is applied in a manner similar to that used for gilding or silvering; the pills having been evenly dampened with a very thin adhesive liquid (mucilage of acacia ʒj, syrup ʒj, and water ʒvj, or tragacanth 4 grains, syrup ʒss, and water ʒviiss), are rotated in a globular box with purified talcum or a mixture of talcum and sugar in the form of an impalpable powder. If a high polish is desired, this can be obtained by rotating them afterward in another globe coated on the inside with paraffin.

Enteric Pills.—This name has been applied to pills which are intended not to disintegrate or dissolve in the stomach, but to undergo solution in the alkaline fluids of the intestines. To insure perfect protection against action of the gastric juice, such pills must be coated with some material, which itself is not affected until the intestinal tract is reached, and for this purpose coating with keratin was first proposed. Keratinized pills were first introduced by Dr. Unna, of Germany, but have not met with much favor, on account of the tedious process of coating. Keratin is a constituent of all horny matter, and is obtained from the same, after removal of fat with ether, by digestion, in the form of shavings or turnings with a mixture of pepsin, hydrochloric acid, and water, for twenty-four or thirty-six hours: this treatment removes all matter soluble in the gastric juice. The residue, having been well washed with water, is digested with 8 or 10 times its weight of 5 per cent. ammonia water in a loosely stopped fiask, at a moderate heat, until a nearly complete solution results, which is then filtered and evaporated to dryness. Keratin, as thus prepared, is a commercial article; both acid and alkaline solutions of it are used for coating pills.

Ammoniacal solution of keratin is prepared by dissolving 7 parts of keratin in a mixture of 50 parts of 10 per cent. ammonia water and 50 parts of 60 per cent. alcohol (solution may be facilitated by warming). This alkaline solution should be used for pills containing trypsin, pancreatin, metallic sulphides, etc.

Acetic solution of keratin, made by dissolving 7 parts of keratin in 100 parts of glacial acetic acid (if necessary, by the aid of a moderate heat), is adapted for pills containing ferric chloride, tannin, salicylic acid, arsenic, creosote, and the salts of mercury, gold, and silver.

For chemically indifferent substances, either the alkaline or acid solution of keratin may be employed.

All pills intended to be coated with keratin should be made with

some fatty excipient and contain no appreciable moisture; the mass is best made with cacao butter and oil of sweet almond, or a mixture of purified mutton tallow or cacao butter 10 parts and white or yellow wax 1 part. After the pills have been rounded they should be dipped in melted cacao butter, which is allowed to harden; they are then placed in a porcelain dish, the keratin solution added (about 30 or 40 drops for 100 pills of medium size) and rotated until the pills have become thoroughly moistened, after which they are dried on parchment paper, to which they will not adhere. The application of keratin solution must be repeated three or four times and allowed to dry each time.

The above process is tedious, and in the majority of cases the following shorter method, proposed by Dunning, will be found entirely satisfactory: 1 Gm. of keratin is rubbed to a smooth paste with 6 mils. (or Cc.) of spirit of ammonia and warmed, while a few drops of water, sufficient to produce a clear solution, are added. The pills do not require a coating of cacao butter, and having been made hard and dry are placed on the points of fine needles, and immersed one at a time in the solution, which is kept warm, the loss by evaporation being made up by addition of spirit of ammonia and a little water. After immersion in the solution, the pill is held in such a position that the drop forming on the under surface may be removed by a piece of cardboard, after which the needle is rotated for a few moments and then pushed through a piece of cardboard standing vertically, for the purpose of drying the pills. The minute orifice left by the needle-point is subsequently closed with a little of the keratin solution. This plan is especially adapted to a small number of pills, 12 to 30, at the dispensing counter.

Phenyl salicylate, or salol, being, like keratin, insoluble in the gastric juice, has also been recommended for coating pills not to be dissolved or disintegrated until the bowels are reached. In order to be efficient 3 separate coatings of salol are usually applied. A sufficient quantity of salol, 10 grains for 30 grains of pill mass, having been melted in a dish on a waterbath, is cooled just short of congealing, when the pills are added and the dish rapidly rotated. The second coating requires about the same quantity of salol, which is also fused and applied a little warmer than the first. Lastly, a smaller quantity of salol, about two-thirds of the first quantity, is used in the same manner. Finally, in order to produce a smooth finish the pills are rapidly rotated in another portion of salol, about 3 grains for 20 three-grain pills, fused and applied while quite warm, the rotation being continued until the pills are cold.

THE OFFICIAL PILLS.

The U. S. Pharmacopœia gives working formulas for 7 varieties of pill masses, and as these are directed to be divided into a definite

number of pills, they are indicated under the title "Pilulæ." The term "Massa" is applied to those combinations which are intended to be kept on hand in bulk, being frequently prescribed as constituents of other pill masses. In the British Pharmacopœia formulas for pill masses only are given, but in no case is the mass directed to be divided into a given number of parts; they are all designated by the simple title "Pilula."

ALPHABETICAL LIST OF THE OFFICIAL PILLS.

Latin name.	English name.	Composition of each pill.		
Pilulæ:				
Aloes	Pills of Aloes	Aloes	0.13	Gm.
		Soap	0.13	"
		Water, a sufficient quantity.		
Asafœtidæ	Pills of Asafetida	Asafetida	0.20	Gm.
		Soap	0.06	"
		Water, a sufficient quantity.		
Catharticæ Compositæ	Compound Cathartic Pills	Comp'd Extract of Colocynth	0.08	Gm.
		Mild Mercurous Chloride	0.06	"
		Resin of Jalap	0.02	"
		Gamboge	0.015	"
		Diluted Alochol, a sufficient quantity.		
Ferri Carbonatis	Pills of Ferrous Carbonate (Blaud's Pills) (Ferruginous Pills) (Chalybeate Pills)	Ferrous Sulphate, crystalliz'd	0.16	Gm.
		Potassium Carbonate	0.08	"
		Sugar	0.04	"
		Tragacanth	0.01	"
		Althæa	0.01	"
		Glycerin and Water, a sufficient quantity.		
Ferri Iodidi	Pills of Ferrous Iodide	Reduced Iron	0.04	Gm.
		Iodine	0.05	"
		Glycyrrhiza	0.04	"
		Sugar	0.04	"
		Extract of Glycyrrhiza	0.01	"
		Acacia	0.01	"
		Water, a sufficient quantity.		
Phosphori	Pills of Phosphorus	Phosphorus	0.0006	Gm.
		Althæa	0.060	"
		Acacia	0.060	"
		Glycerin and Water, a sufficient quantity.		
Rhei Compositæ	Compound Pills of Rhubarb	Rhubarb	0.13	Gm.
		Aloes	0.13	"
		Myrrh	0.06	"
		Oil of Peppermint	0.005	Cc.
		Water, a sufficient quantity.		

The *National Formulary* gives directions for making 32 different pills, the formula in each case calling for 100 pills, and a suitable excipient being named. The following list gives the composition of the different pills:

Latin name.	English name.	Composition.
Pilulæ ad Prandium	Dinner Pills	Although the name Dinner Pill is generally applied to the Pill of Aloes and Mastic, three other varieties are recognized in the N. F., as follows:
	Chapman's Dinner Pill	Contain aloes, mastic, ipecac, and oil of fennel.
	Cole's Dinner Pill	Contain aloes, mass of mercury, jalap, and antimony and potassium tartrate.
	Hall's Dinner Pill	Contain aloes, extract of licorice, soap, and syrup.

Latin name.	English name.	Composition.
Pilulæ Aloes et Asafœtidæ	Pills of Aloes and Asafetida	Contain aloes, asafetida and soap.
Pilulæ Aloes et Ferri	Pills of Aloes and Iron	Contain aloes, exsiccated ferrous sulphate and aromatic powder, the mass being made with confection of rose.
Pilulæ Aloes et Mastiches	Pills of Aloes and Mastic (Lady Webster's Dinner Pills)	Contain aloes, mastic and red rose.
Pilulæ Aloes et Myrrhæ	Pills of Aloes and Myrrh	Contain aloes, myrrh and aromatic powder.
Pilulæ Aloes et Podophylli Compositæ	Compound Pills of Aloes and Podophyllum (Janeway's Pills)	Contain aloes, resin of podophyllum, extract of belladonna leaves, and extract of nux vomica.
Pilulæ Aloes, Hydrargyri et Podophylli (Pilulæ Triplices)	Pills of Aloes, Mercury and Podophyllum (Triplex Pills)	Contain aloes, blue mass and resin of podophyllum.
Pilulæ Aloes, Hydrargyri et Scammonii Compositæ	Compound Pills of Aloes, Mercury and Scammony (Francis' Triplex Pills)	Contain aloes, resin of scammony, blue mass, croton oil and oil of caraway, the mass being made with tincture of aloes and myrrh.
Pilulæ Aloini Compositæ	Compound Pills of Aloin	Contain aloin, resin of podophyllum, and extract of belladonna leaves.
Pilulæ Aloini, Strychninæ, et Belladonnæ	Pills of Aloin, Strychnine, and Belladonna	Contain aloin, strychine (alkaloid), and extract of belladonna leaves.
Pilulæ Aloini, Strychninæ, et Belladonnæ Compositæ	Compound Pills of Aloin, Strychnine, and Belladonna	Contain aloin, strychnine (alkaloid), extract of belladonna leaves, and extract of cascara sagrada.
Pilulæ Antidyspepticæ	Antidyspeptic Pills	Contain strychnine (alkaloid), ipecac extract of belladonna leaves, mass of mercury, and compound extract of colocynth.
Pilulæ Antimonii Compositæ	Compound Pills of Antimony (Plummer's Pills)	Contain sulphurated antimony, calomel and guaiac, the mass being made with castor oil.
Pilulæ Antiperiodicæ	Antiperiodic Pills (Warburg's Pills)	Contain extract of aloes, rhubarb, angelica seed, elecampane, saffron, fennel, zedoary root, cubebs, camphor, myrrh, white agaric, quinine sulphate, and extract of gentian.
Pilulæ Antiperiodicæ sine Aloe	Antiperiodic Pills without Aloes (Warburg's Pills without Aloes)	Contain the same ingredients as the preceding pills, excepting the extract of aloes.
Pilulæ Catharticæ Vegetabiles	Vegetable Cathartic Pills	Contain compound extract of colocynth, extract of hyoscyamus, resin of jalap, extract of leptandra, resin of podophyllum and oil of peppermint.
Pilulæ Colocynthidis Compositæ	Compound Pills of Colocynth	Contain extract of colocynth, aloes, resin of scammony, and oil of cloves. These pills are also known as Cochia Pills.
Pilulæ Colocynthidis et Hyoscyami	Pills of Colocynth and Hyoscyamus	Contain extract of colocynth, aloes, resin of scammony, oil of cloves, and extract of hyoscyamus.
Pilulæ Colocynthidis et Podophylli	Pills of Colocynth and Podophyllum	Contain extract of colocynth and resin of podophyllum.

Latin name.	English name.	Composition.
Pilulæ Digitalis, Scillæ et Hydrargyri . .	Pills of Digitalis, Squill and Mercury (Niemeyer Pills for Dropsy, Guy's Pills) .	Contain digitalis, squill and blue mass.
Pilulæ Ferri, Quininæ, Aloes et Nucis Vomicæ (Pilulæ Quadruplices, Pilulæ Ferri et Quininæ Compositæ)	Pills of Iron, Quinine, Aloes and Nux Vomica (Quadruplex Pills, Quatour Pills) . . .	Contain exsiccated ferrous sulphate, quinine sulphate, aloes and extract of nux vomica, the mass being made with extract of gentian.
Pilulæ Ferri, Quininæ, Strychninæ et Arseni Fortiores (Pilulæ Metallorum, Pilulæ Metallorum Amaræ)	Stronger Pills of Iron, Quinine, Strychnine and Arsenic (Metallic Pills, Bitter Metallic Pills)	Contain reduced iron, quinine sulphate, strychnine and arsenic trioxide.
Pilulæ Ferri, Quininæ, Strychninæ et Arseni Mites	Mild Pills of Iron, Quinine, Strychnine and Arsenic (Aitken Tonic Pills) . . .	Contain reduced iron, quinine sulphate, strychnine and arsenic trioxide.
Pilulæ Glycerylis Nitratis (Pilulæ Glonoini	Pills of Nitroglycerin (Pills of Glonoin) . .	Contain spirit of glyceryl trinitrate and althæa, the mass being made with confection of rose.
Pilulæ Laxativæ Compositæ	Compound Laxative Pills . .	Contain aloin, strychnine, extract of belladonna leaves, ipecac and glycyrrhiza.
Pilulæ Laxativæ Postpartum	Laxative Pills after Confinement (Barker's Postpartum Pills)	Contain compound extract of colocynth, Socotrine aloes, extract of nux vomica, resin of podophyllum, ipecac and extract of hyoscyamus.
Pilulæ Opii, Digitalis et Quininæ . . .	Pills of Opium, Digitalis and Quinine (Niemeyer Pills for Phthisis) . .	Contain opium, digitalis and quinine sulphate.
Pilulæ Opii et Camphoræ	Pills of Opium and Camphor . .	Contain powdered opium and camphor.
Pilulæ Opii et Plumbi	Pills of Opium and Lead . . .	Contain powdered opium and lead acetate.
Pilulæ Rhei . . .	Pills of Rhubarb	Contain rhubarb and soap.

SPECIAL REMARKS.

If it is desired to keep any of the official pills in stock in an uncoated condition, they should at once be placed in a mixture of lycopodium and powdered licorice root, and allowed to remain there until dry, which may require from four to eight days; they can then be kept in bottles without danger of moulding or losing their shape. This plan is particularly advisable for the Compound Cathartic Pills.

Compound Cathartic Pills.—In making these well known pills powdered resin of jalap is to be preferred to the pilular extract formerly directed; it should first be mixed with the gamboge and calomel and finally with the powdered compound extract of colocynth. A moderate quantity of water (f℥vj for 1000 pills), which should be added to the mixed powders all at once, suffices to make a satisfactory firm mass, provided the mixture be well kneaded in the mortar.

Compound Cathartic Pills should never be put into stock bottles until perfectly dry and hard.

Pills of Ferrous Carbonate.—Blaud's pills, as the official pills of ferrous carbonate are more commonly termed, have probably caused inexperienced pharmacists more trouble than any other pill mass; this is partly owing to the fact that physicians frequently order equal parts of ferrous sulphate and potassium carbonate, which render the mass very deliquescent, on account of the excess of potassium carbonate. The official directions are to triturate the iron salt and sugar together, and add this mixture to the potassium carbonate previously rubbed smooth with glycerin and water (10 drops of each for every 100 pills); the mass is thoroughly triturated until it assumes a green color, and is then incorporated with the tragacanth and althæa, a little more water being added if necessary. The formula yields satisfactory results, the secret of success lying in the completed reaction between the iron and potassium salts before the final massing with tragacanth and althæa. The mass should be rolled out and cut while still moderately soft. The official formula is based on the assumption that absolutely pure potassium carbonate will be used, in which case the decomposition will be complete, as the 16 Gms. of crystallized ferrous sulphate require 7.954 Gms. of potassium carbonate, yielding 6.673 Gms. of ferrous carbonate. If the potassium carbonate used be less than 100 per cent. pure, slight excess of ferrous sulphate will be present.

Mr. H. B. Dunning, of Baltimore, has suggested the following modification of the pharmacopœial formula, which eliminates the tragacanth and althæa, as these have a tendency to make the pills tough and hard. Take of Ferrous Sulphate crystals 15 Gms., Potassium Carbonate 8.75 Gms., Sugar 1.25 Gms., Powdered Glycyrrhiza 6.25 Gms. Rub the iron and sugar into fine powder, add the potassium carbonate previously powdered, and mix with 40 minims of water. Triturate the mixture until dry and in powder, add the glycyrrhiza and sufficient glucose to make a smooth mass, which divide into 100 pills. Pills made by this formula retain their shape and green color for a long time (over three months in paper boxes), and while assuming a darker color on the outside, due to gradual drying, the interior remains fairly soft.

Physicians sometimes prescribe 4 drachms each of ferrous sulphate and potassium carbonate to be made into 100 pills, which proportions should be changed to 4 drachms and 140 grains, respectively. In such cases the following method of procedure has been used with marked success for many years: Rub the 240 grains of crystallized ferrous sulphate into a fine powder with 30 grains of sugar, and mix with 140 grains of potassium carbonate also reduced to powder; the mixture, which will soon soften and change color, should be stirred from time to time until the reaction is complete, which is known by the disappearance of the granular condition and the formation of a green,

smooth, very soft paste. Now add 30 grains each of powdered starch and powdered acacia, mass quickly, and roll out while still soft, as the mass rapidly becomes firm, and may then crumble when rolled out.

Blaud's pills are intended to contain about 0.0667 Gm. (about 1 grain (of ferrous carbonate, and cannot be kept on hand uncoated on account of the tendency to rapid oxidation of the iron salt, which is retarded, but not entirely obviated, by the sugar or sugar and glycerin present. The pills should be of a uniform deep green color, and are best prepared fresh when wanted. In Great Britain the mass for Blaud's pills is officially recognized by the simple term "Pilula Ferri," and its composition is about the same as that published in our own Pharmacopœia.

Pills of Ferrous Iodide.—The first step in the manufacture of pills of ferrous iodide is to mix the reduced iron with water (6 mils. (or Cc.) for 100 pills), then adding the iodine, and stirring until the reddish tint of the mixture disappears. The glycyrrhiza, acacia, and sugar are now added, and after thorough admixture the whole is evaporated on a waterbath to a pilular consistence. The official pills are presumably identical with Blancard's Pills; they contain an excess of iron, which aids in their preservation. Each pill is designed to contain about 0.0610 Gm. (about 1 grain) of ferrous iodide. Owing to the heat generated by the union of the iodine with the finely divided iron, the former should be added slowly, so as to avoid loss by vaporization, and the mixed powders should not be added until all traces of free iodine have disappeared. When the mass has been evaporated to a proper consistence on a waterbath it will weigh about 20 Gms. The 5 Gms. of iodine ordered in the official formula require 1.104 Gm. of absolutely pure iron to form ferrous iodide; the amount of iron in excess will therefore depend upon the purity of the reduced iron used.

Since pills of ferrous iodide are not, as a rule, made extemporaneously, and are readily affected by air and moisture, the Pharmacopœia very properly directs a resinous coating to be applied; a modified form of tolu solution, which has been found preferable to the official ethereal solution, has already been referred to on page 417.

Pills of Phosphorus.—The official directions for making pills of phosphorus are to dissolve the carefully weighed phosphorus in chloroform (5 mils. (or Cc.) for 100 pills) contained in a test-tube, heating gently if necessary to facilitate solution. Mix the althæa and acacia, add the solution of phosphorus, then immediately afterward a mixture of glycerin 2 volumes and water 1 volume (4 mils. (or Cc.) for 100 pills), and quickly form the mass. The uniform distribution of phosphorus in a pill mass is best effected in a state of solution, and the choice of chloroform as a solvent in the official formula has a double advantage. Chloroform, besides being one of the best solvents for phosphorus known, is readily dissipated, owing to its very volatile nature, leaving the phosphorus, in a very finely divided form, intimately distributed throughout the mixed powders, while its heavy, non-

inflammable vapor hovers over the mortar during the making of the pill mass, thus protecting the phosphorus against oxidation. Phosphorus, being very inflammable, must be cut and weighed under water, hence the weighing of small quantities is often attended with much difficulty. A small glass capsule or a watch-crystal, containing some water, should be carefully tared, and in it the phosphorus, having been cut into small pieces under water with a penknife, should be weighed; the pieces may be removed with a small pair of forceps, quickly dried by means of filter paper, and then dropped into the chloroform contained in a test-tube.

Phosphorus is rapidly oxidized, particularly in a state of fine division; hence pills of phosphorus should be coated as soon after they have been made as possible; as in the case of pills of ferrous iodide, the modified solution of balsam of tolu is preferable to the official ethereal solution.

The official method for incorporating phosphorus in a pill mass may also be followed when phosphorus is ordered in combination with other remedial agents, such as quinine sulphate, extract of nux vomica, etc. If phosphorus be extensively used in pill form, another plan is to prepare a 10 per cent. intimate mixture of phosphorus and rosin, as follows: Weigh off 1 Gm. of phosphorus and melt the same by placing it in a mortar containing hot water (not boiling); now add 9 Gms. of rosin, which softens in the hot water, and mix the phosphorus and rosin *intimately* by triturating and kneading. Pour off the water and preserve the phosphoretted resin, after it has been dried between filter paper, in a small, tightly stoppered bottle in a dark place. Each gram of this preparation represents 0.100 Gm. of phosphorus, or 10 grains equal 1 grain, and may be conveniently weighed without danger of ignition. It keeps well for some time, but gradually the phosphorus becomes oxidized, the change beginning on the exterior and slowly extending inward.

Compound Pills of Rhubarb.—Compound pills of rhubarb will become very hard by age, and as they are not often called for, it is decidedly better to keep the ingredients properly mixed, in a glass-stoppered bottle, and make the mass when required. A mixture of syrup and water, or glycerin and water, may be used with advantage in place of water, as in the case of pills of aloes and mastic.

THE OFFICIAL MASSES.

As stated before, these masses are usually employed as constituents of other pill masses; they are Massa Ferri Carbonatis and Massa Hydrargyri. The latter only is of sufficiently firm consistence to admit of being rolled into pills which will retain their spherical shape without the addition of absorbents, except when freshly made in warm weather.

Massa Ferri Carbonatis; *Mass of Ferrous Carbonate*, also known as *Vallet's Mass*, is a mixture of ferrous carbonate, sugar, and honey. Even when very carefully made, so as to contain the full amount of iron salt, it is never of a pilular consistence, but always in the form of a rather tenacious paste. The Pharmacopœia directs the preparation of ferrous carbonate by mixing cooled and filtered solutions of ferrous sulphate and sodium carbonate, made respectively with crystallized ferrous sulphate 100 Gms., boiling distilled water 200 mils. (or Cc.) and syrup 20 mils. (or Cc.), and monohydrated sodium carbonate 46 Gms. and boiling distilled water 200 mils. (or Cc.) and then washing the resulting precipitate well with sweetened water (syrup 1 volume, distilled water 19 volumes) until the newly formed sodium sulphate has been removed; the washing is best performed by decantation in flasks having a narrow neck, and which can be tightly stoppered. The precipitate is then drained on a strainer, mixed with clarified honey 38 Gms. and sugar 20 Gms., and the whole evaporated in a tared capsule, with constant stirring, until reduced in weight to 100 Gms.

The iron solution should be poured slowly into the alkaline solution and the flask frequently rotated as long as carbon dioxide escapes, after which it is filled with distilled water, corked, and set aside. The object of adding syrup to the iron solution, and of the subsequent washing of the precipitate with sweetened water, is to prevent oxidation of the iron salt as far as possible. Instead of distilled water, pure river or spring water recently boiled may be used throughout the process.

Theoretically the official product should contain about 42 per cent. of ferrous carbonate, as 100 Gms. of crystallized ferrous sulphate will yield 42 Gms. of the carbonate, but as there is always some loss during the washing process, the finished mass rarely contains more than 36 per cent., and this much only if care has been observed to prevent oxidation by rigid exclusion of air. The Pharmacopœia requires that mass of ferrous carbonate, when assayed, shall contain not less than 35 per cent. of the ferrous compound. Freshly precipitated ferrous carbonate is greenish-gray, gradually deepening in color, and the finished mass is decidedly green, but should not be brown, which would indicate oxidation. When Vallet's mass is allowed to stand for some time, even in well-covered jars, it becomes dry on the surface and assumes a blackish-green color. The change extends to the interior very slowly, being due to the gradual escape of moisture.

Massa Hydrargyri; *Mass of Mercury*, better known as *Blue Mass* or *Blue Pill*, is probably the most familiar of all pill masses. In the official formula 33 Gms. of mercury are triturated with 1 Gm. of oleate of mercury in a warm mortar, after which 32 Gms. of honey of rose and 9 Gms. of glycerin are incorporated. When globules of mercury are no longer visible under a lens magnifying 10 diameters, 10 Gms. of powdered licorice root and 15 Gms. of powdered althæa are gradually added and the trituration continued until a homogeneous

mass is obtained. Blue mass contains 33 per cent. of metallic mercury, which probably undergoes slight superficial oxidation in the course of time, but is well protected by the other ingredients.

The Pharmacopœia requires that blue mass, when assayed, shall contain not less than 32 per cent., nor more than 34 per cent. of mercury.

The *National Formulary* gives directions for making a pill mass, which was at one time official in the Pharmacopœia.

Massa Copaibæ; *Mass of Copaiba*, also known as *Solidified Copaiba.*—The formation of this mass depends upon the reaction between an acid resin present in copaiba and hydrated magnesium oxide. Thin fluid copaiba, rich in volatile oil, is not well adapted for making this mass, which should be of pilular consistence, but the directions to heat the mixture of copaiba and magnesia on a waterbath for half an hour improves the condition; thick copaiba, containing more resin and less oil, will yield a good mass even without application of heat.

CHAPTER XXIX.

CONFECTIONS AND LOZENGES.

CONFECTIONS.

THIS class of medicinal preparations still finds recognition in the leading pharmacopœias, although, in this country at least, they are very rarely used by physicians. At one time the incorporation of saline and vegetable remedial agents with honey or fruit pulp was a favorite mode of medication, such being the invariable composition of electuaries or confections, which were dispensed in the form of a thick, semifluid mass. When made with honey, or with the addition of glycerin, confections retain their original soft condition for a long time; but if made with fruit pulp, or sugar and water, the moisture gradually evaporates and the mass becomes dry and hard. All medicinal ingredients must be added in the form of impalpable powder, and heavy metallic salts should never be employed, as they are prone to sink to the bottom and thus become separated. Whenever essential oils are to be incorporated in confections, they should first be triturated thoroughly with some finely powdered sugar; narcotic extracts or other potent remedies should be added in the form of solution, so as to insure their uniform distribution throughout the soft mass.

Confections are no longer recognized in our Pharmacopœia, but the two heretofore official have been introduced into the *National Formulary*. The British Pharmacopœia still retains four confections, namely: *Confection of Pepper, Confection of Roses, Confection of Senna, Confection of Sulphur*, while the German and Swiss Pharmacopœias recognize but one confection, designated as *senna electuary*.

Confectio Rosæ.—Confection of rose, which at one time was largely used as a favorite excipient for certain pill masses, possesses little or no medicinal virtue. The *National Formulary* directs it to be made by rubbing red rose leaves, in No. 60 powder, with stronger rose water, previously heated to 65° C. (149° F.), for the purpose of reducing the rose petals to a pulpy condition, and then gradually adding clarified honey and finely powdered sugar.

Confectio Sennæ.—Confection of senna, sometimes called for under the name of *lenitive electuary*, if carefully prepared, presents an agreeable, mild laxative preparation. The *National Formulary* directs that tamarind, sliced prune, bruised fig, and bruised cassia fistula be digested with water for three hours on a waterbath. The coarser portions are then to be separated and the pulpy mass rubbed first

through a coarse hair sieve, and then through a fine one or through a muslin cloth. If the digestion be carried on on a boiling waterbath for three hours, with occasional stirring by means of a thick glass rod or a porcelain spatula, the pulpy mixture can easily be passed through a hair sieve with the aid of a horn spatula. The residue remaining in the sieve is again digested for a short time with water, the mixture treated as before, and the product added to the pulpy mass first obtained. Sugar is then dissolved in the pulpy liquid and the whole evaporated to 89.5 per cent. of the intended weight of finished product, to which while yet warm are added senna, in No. 60 powder, and oil of coriander. It will be found advisable, instead of adding the oil directly with the senna to the pulp, to triturate it thoroughly first with a small portion of sugar, which should be reserved for that purpose out of the original quantity.

LOZENGES OR TROCHES.

Lozenges are solid, flattened masses of round, oval, or other desirable shape, not intended for mastication, but to be dissolved slowly in the mouth, therefore not adapted for medicines which are expected to undergo disintegration in the stomach prior to any therapeutic action. In one or two cases the cylindrical form is preferred, as for the well known licorice lozenges and Wistar's cough lozenges. The remedial action of lozenges is generally designed to be purely local, either as an expectorant, demulcent, stimulant, sedative, astringent, or antiseptic.

The usual base or vehicle for lozenges is sugar (that known among confectioners as lozenge sugar being preferred), although powdered extract of licorice also is added at times, and, of late years, fruit paste, made from black or red currants, has come extensively into use for certain kinds of lozenges. Adhesiveness is obtained by the addition of tragacanth or acacia, and syrup or water (plain or aromatic) is used to supply the necessary moisture. All medicinal constituents, as well as the sugar or extract of licorice should be in very fine powder to insure a smooth paste, and potent remedies, wherever possible, should be added either in the form of solution or triturated with a small quantity of sugar before being mixed with the other ingredients, so as to insure uniform distribution. Tragacanth is preferable to acacia for making a lozenge mass, as the resulting paste is more tenacious; in both cases the mucilage is to be preferred to the powder with the subsequent addition of water, as in the latter case it is often difficult to avoid an excess of moisture, which retards subsequent drying.

The British Pharmacopœia (1914) directs acacia as the adhesive agent for lozenges in all cases but one, and designates four distinct bases or vehicles of the following composition: *Simple basis*—sugar 496 Gms., powdered acacia 19.5 Gms., mucilage of acacia 35 milliliters, distilled water a sufficient quantity. *Fruit basis*—sugar 26 Gms.,

powdered ragacanth 6.5 Gms., black-currant paste a sufficient quantity to produce 650 Gms. *Rose basis*—sugar 496 Gms., powdered acacia 19.5 Gms., mucilage of acacia 35 milliliters, oil of rose 0.025 milliliter, distilled water a sufficient quantity. *Tolu basis*—sugar 482 Gms., powdered acacia 19.5 Gms., mucilage of acacia 35.5 Cc., tincture of tolu 10 milliliters, distilled water a sufficient quantity. Instead of giving individual formulas for making the 17 varieties of lozenges recognized, a general formula, adjusted for 500 lozenges, is given under the head of each basis, as follows: 500 times the quantity of medicinal agent required for one lozenge is intimately mixed with the sugar and acacia, and a paste then made with the other ingredients, which is divided into 500 equal parts and dried at a moderate temperature.

Lozenge masses are made after the manner of pill masses, except that more adhesive material is used, and the paste is made somewhat softer. The proportion of powdered tragacanth necessary for a well made plastic mass may vary from 1 to 3 per cent. of the total weight of the mixed powders (acacia about three or four times as much); and in making the mass the necessary water or syrup should be added cautiously, and the mixture well kneaded after each addition, so as to avoid too soft a condition, which readily occurs on account of the great solubility of the sugar. A good plan is to follow the suggestion of Hager, to reserve about one-fifth of the powder, and when the remaining four-fifths have been made into a plastic mass, quickly incorporate the reserve portion, which can be done without risk of the mass becoming dry and crumbly. For massing small quantities of material a Wedgwood mortar and pestle will be found quite convenient, while for large quantities the pill mass mixers shown on page 396 are preferable.

After a suitable mass has been made, it is transferred to a hard wood board or a stone slab, rolled out into either a flat sheet or a cylinder, and divided into the requisite number of parts. When cylindrical lozenges are to be made, the mass is rolled out without dusting, and divided into pieces about five-eighths of an inch in length, by means of a special cutter. In order to prevent the mass from adhering the flat roller may be lightly rubbed with a very small quantity of oil of sweet almond. For flat lozenges the mass is conveniently rolled out into a sheet, the required thickness of which must be ascertained by experiment; this is done by dividing the weight of the whole mass by the number of lozenges to be made, then weighing off as many grains of the mass as correspond to the quotient obtained, and forming this into a lozenge by means of a punch or spatula. As every well made lozenge board is provided with guides and screws for regulating different thicknesses, no difficulty will be experienced in adjusting the side strips to the proper height, and then rolling out the mass by means of a cylindrical roller, as shown in Fig. 261. To prevent adhesion of the mass, the board may be dusted with a little starch or a mixture of starch and sugar.

The lozenge board designed by Wallace Procter is very useful and simple in construction, as shown in Fig. 262. *A* is a board of well

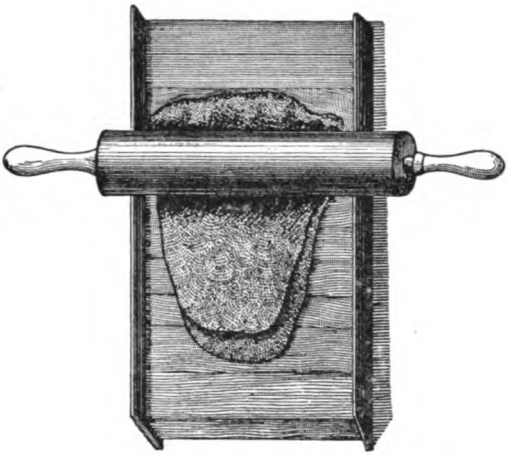


FIG. 261.—Showing the manner of rolling out the lozenge mass.

seasoned hard wood, $1\frac{1}{2}$ inches thick, 10 inches wide, and 14 inches long, planed perfectly flat, and both sides and ends made square and true. At each side, about 3 inches from one end, a plate is let

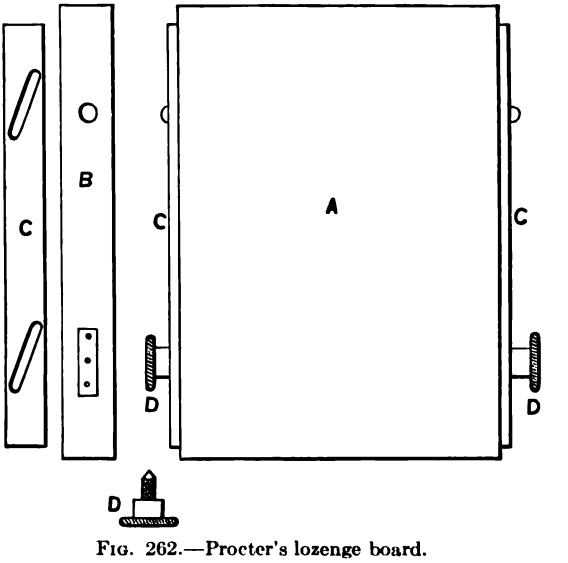


FIG. 262.—Procter's lozenge board.

in flush and tapped with a screw, as shown in *B*. On each side of the board a plate of brass, $1\frac{1}{2}$ inches wide, 14 inches long, and $\frac{3}{16}$

of an inch thick, is fitted. Each plate has two slots crossing it diagonally (see *C*) $\frac{3}{8}$ of an inch from each edge; these slots must have exactly the same slope, and the front slot should be ruled to divisions of $\frac{1}{10}$ of an inch. Through one slot of each plate a square-shouldered screw passes, and is screwed in until it presses the plate close to the side of the board, but still permits it to move easily; through the other slot in each plate passes a set-screw, which enters the screw-plate

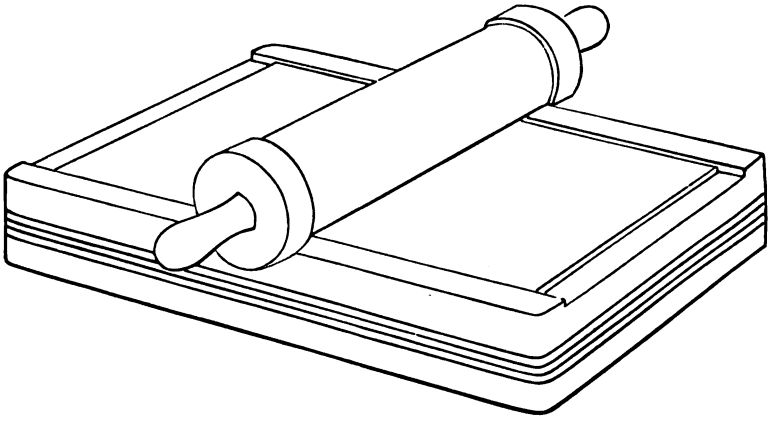


FIG. 263.—Harrison's lozenge board.

before mentioned. When the plates have been adjusted to a given height the set-screws are turned until they prevent motion of the plate.

Harrison's lozenge board (see Fig. 263), which has been known oor many years, consists of two frames of wood, of which one moves forward and backward inside of the other in grooves cut into the futer frame; the board on which the mass is rolled rests firmly on the inner frame, and has fastened to its bottom two bevelled strips

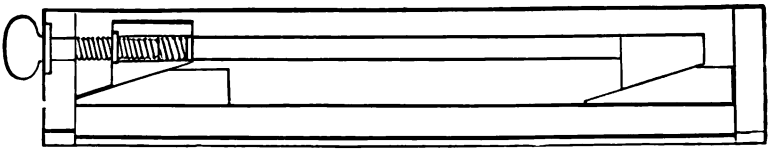


FIG. 264.—Harrison's lozenge board (sectional view).

corresponding to similar strips attached to the frame. By means of a screw the inner frame can be pushed forward, and the board thus forced upward (see Fig. 264). As the bevels give $\frac{3}{8}$ of an inch rise, for which 15 complete revolutions of the screw are required, each half-turn of the screw will cause a rise of $\frac{1}{80}$ of an inch; in this way any required thickness of the mass can be obtained. The outer frame is stationary, the sides projecting $\frac{3}{8}$ of an inch above the ends, and

serving as a support for the rolling pin, which is also provided with a flange at each end to keep it in proper position. While the rolling pins are usually made of wood, steel or glass rollers may also be used, the former being particularly desirable when heat is to be employed.

The punches used for cutting lozenges are usually in the form of tapering cylinders made of heavily tinned iron, and frequently provided with sharp cutters of hardened steel, the shape of which varies with the fancy of the operator; sometimes they are made with straight sides and fitted with a plunger, operated by a spring, for the ready expulsion of the lozenges. Figs. 265, 266, and 267 represent some of the usual styles. In large manufacturing establishments ten or twelve

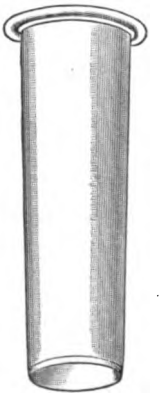


FIG. 265.—Plain tin lozenge cutter.

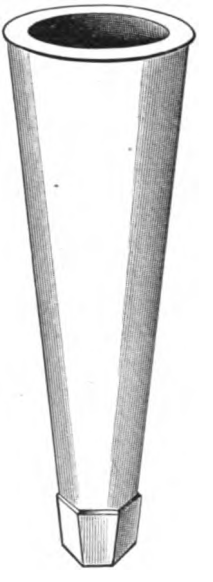


FIG. 266.—Tin lozenge punch with steel cutter.

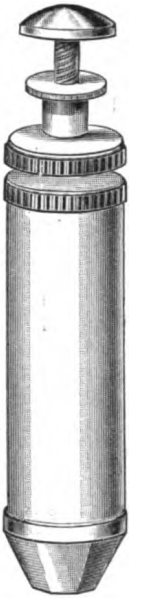


FIG. 267.—Lozenge punch with spring.

cutters are frequently combined and operated as one, greatly expediting the work. Whenever it is desired to stamp lozenges with some special letter or design, this is done at the time of cutting them, the plunger being provided with the necessary die.

As the preparation of lozenges has almost entirely passed out of the hands of the retail pharmacist, very few stores are now provided with suitable appliances for making them. When a small number of lozenges is wanted extemporaneously, a stiff mass should be made in order to facilitate subsequent drying; it may then be rolled out on a pill machine or pill tile, to be cut into the requisite number of parts, each of which should be given a globular shape and then flattened into a suitable disk, for which purpose the simple apparatus

shown in Fig. 268 will be found very convenient. This consists of a brass or steel tube, about 2 or 3 inches long, $\frac{3}{8}$ to $\frac{5}{8}$ of an inch in diameter, and of $\frac{1}{8}$ or $\frac{3}{16}$ of an inch in thickness; the bore of the tube must be uniform and smooth and the ends square, otherwise the lozenges will present an irregular appearance. A plunger accurately fitting the tube, preferably made of the same metal, is necessary; it should be of the same length as the tube, and provided with a top about an inch long, exactly covering the outside diameter of the tube. It is desirable that both parts be nickel-plated. To shape the lozenges properly, the globular mass, slightly dusted with starch and sugar or lycopodium, is placed in the cylinder, resting upon a metallic base, which consists of a nickel-plated piece of steel or brass, about 2 inches square and $\frac{1}{4}$ inch thick, set in a block of hard wood (see Fig. 266); the plunger having been inserted, it is struck a quick, sharp blow with a mallet, after which the cylinder is raised and the lozenge expelled by lightly tapping the plunger with the mallet. The apparatus shown on page 443, Fig. 273, may also be employed for shaping lozenges, although it is inferior to the above for compressing masses, owing to the projection of the base into the cylinder.

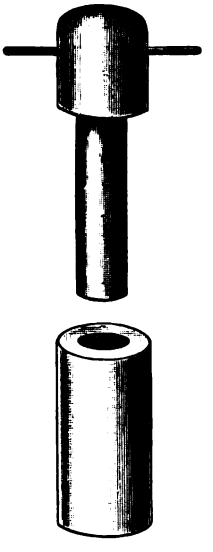


FIG. 268.—Lozenge apparatus.

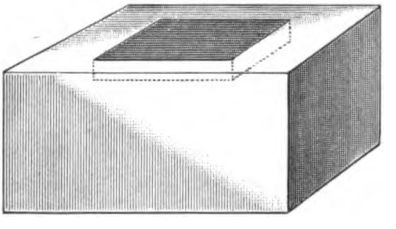


FIG. 269.—Base for lozenge apparatus.

In Fig. 270 is shown a lozenge-cutting machine, operated by power, and having a capacity of 300 lozenges a minute. The mass or dough having been previously rolled into a sheet is placed on the conveyer belt and the machine is set in motion, when the mass is moved forward under a finishing roller, which gives it the necessary uniform evenness; the roller can be adjusted to any desired thickness. The mass is then fed automatically under a series of tapering cutters attached to a bar or plate, and the lozenges drop out separately into a receiving tray. The Arthur Colton Co., of Detroit, make a similar machine of large size, having a capacity of 500 lozenges a minute; it works on the same principle as the Stokes machine, except that the cutters move upward through the mass instead of downward.

Gelatin lozenges, variously medicated, have been in use for some

time, more particularly in Europe. They are composed of a mixture of gelatin, glycerin, and water, holding the medicinal ingredient either in solution or simple admixture. The base is often termed glyco-gelatin, and is made by macerating gelatin with water on a waterbath, and then adding glycerin; two kinds, containing different proportions of gelatin and glycerin, are in use. A mixture of gelatin, 1 ounce; orange flower water, $2\frac{1}{2}$ ounces; and glycerin, $2\frac{1}{2}$ ounces (by weight), yields the softer variety, which is very readily soluble in the mouth; whereas a mixture of gelatin, 5 ounces; orange flower water, 6 ounces; and glycerin, 6 ounces (by weight), evaporated to 15 ounces, produces a much firmer mass, dissolving more slowly, but probably better adapted for stock lozenges in this latitude; in the latter case at least twelve hours' maceration should be given the gelatin and water before adding the glycerin and applying heat. Gelatin lozenges must always be made with the aid of heat, and the

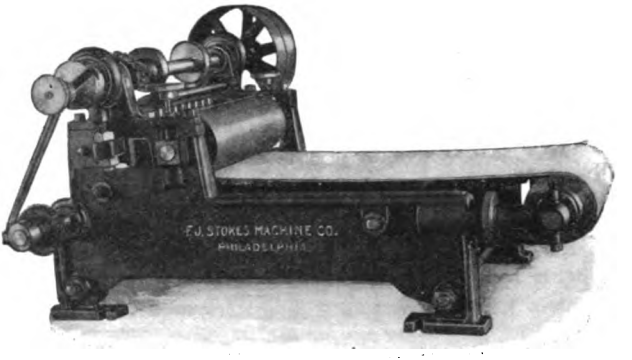


FIG. 270.—Lozenge cutting machine.

mass after thorough admixture with the medicinal ingredients, while still in a melted condition, is poured into suitable moulds, where it rapidly congeals. A very convenient mould for a small number of the lozenges is found in the two side plates of the Konseal filling apparatus shown on page 467. If either of these plates be laid upon a cold porcelain or glass plate, the mixture may be poured directly into the particular perforations selected, and when cold the lozenges are easily removed by being pushed through the perforations. The proper quantity of gelatin mass to use for any particular case is ascertained by filling the perforations with some of the melted plain mass, and when cold weighing the disk; by keeping a memorandum of the weight of such disks much annoyance and labor can be saved. Gelatin lozenges vary in weight from 0.3 to 1.0 Gm. (5 to 15 grains).

Gelatin lozenges, while admirably adapted for the exhibition of such substances, as cocaine, boric acid, carbolic acid, etc., are unsuited for tannin, extract of rhatany, and other agents incompatible with gelatin.

Chocolate lozenges, also known as chocolate tablets and chocolate pastilles, or simply as chocolates, may be conveniently made at the dispensing counter as follows: The medicinal ingredients are intimately mixed with powdered sugar previously flavored with vanilla, Ceylon cinnamon, peppermint, or other flavoring agent (see Oil-sugars), and the mixture then added to three-fourths of its weight of chocolate, in mass or powder, contained in a mortar or porcelain dish. By means of waterbath heat a soft mass is obtained, which is thoroughly mixed, and when cool divided into the requisite number of parts on a lozenge board or a pill tile. Chocolate lozenges vary in weight from 0.3 to 1.0 Gm. (5 to 15 grains), and are not intended to be dissolved slowly in the mouth, but to be swallowed with or without previous mastication.

Lozenges intended for immediate use do not require much drying, but those intended for stock must be thoroughly dried before they are put away in glass containers, otherwise they are liable to soften and adhere, and may even become mouldy. The drying is best effected on perforated trays in a moderately warm room. To avoid cracking of the edges, which will sometimes occur when lozenges are dried, the addition of a small quantity of glycerin to the water used will be found advantageous, and does not interfere with proper desiccation.

The average weight of lozenges is between 0.650 and 1.30 Gm. (10 and 20 grains), although in the five working formulas of the Pharmacopœia the weight is found to vary between 0.40 and 0.96 Gm. (6 and 15 grains).

The following is a list of the official lozenges, showing the composition and excipient used:

LIST OF U. S. PHARMACOPŒIA LOZENGES.

Latin name. Trochisci.	English name.	Composition of each lozenge.
Acidi Tannici	Troches of Tannic Acid	Tannic Acid . . . . . 0.060 Gm. Sugar . . . . . 0.650 " Tragacanth . . . . . 0.020 " Stronger Orange Flower Water, a sufficient quantity.
Ammonii Chloridi	Troches of Ammonium Chloride	Ammonium Chloride . . 0.100 Gm. Extract of Glycyrrhiza . . 0.200 " Tragacanth . . . . . 0.020 " Sugar . . . . . 0.400 " Syrup of Tolu, a sufficient quantity.
Cubebæ	Troches of Cubeb	Oleoresin of Cubeb . . . 0.020 Gm. Oil of Sassafras . . . . 0.010 mil. Extract of Glycyrrhiza . . 0.250 Gm. Acacia . . . . . 0.120 " Syrup of Tolu, a sufficient quantity.
Potassii Chloratis	Troches of Potassium Chlorate	Potassium Chlorate . . . 0.150 Gm. Sugar . . . . . 0.600 " Tragacanth . . . . . 0.030 " Water, a sufficient quantity.
Sodii Bicarbonatis	Troches of Sodium Bicarbonate	Sodium Bicarbonate . . 0.180 Gm. Sugar . . . . . 0.540 " Nutmeg . . . . . 0.010 " Mucilage of Tragacanth, a sufficient quantity.

LIST OF NATIONAL FORMULARY LOZENGES.

Latin name.	English name.	Composition of each lozenge.
Trochisci Carbonis Ligni	Troches of Charcoal	Contain charcoal, tragacanth and sugar, and vanillin as a flavoring.
Trochisci Gambir	Troches of Gambir	Contain gambir, tragacanth and sugar, and oil of cinnamon as a flavoring.
Trochisci Menthæ Piperitæ	Troches of Peppermint	Contain oil of peppermint and sugar, the mass being made with mucilage of tragacanth.
Trochisci Phenolphthaleini	Troches of Phenolphthalein	Contain phenolphthalein, acacia and sugar, and vanillin as a flavoring; the lozenges are colored pink with carmine.
Trochisci Quininæ Tannatis	Troches of Quinine Tannate	Contain quinine tannate, tragacanth, oil of theobroma, prepared cocoa and sugar, and vanillin as a flavoring; 0.002 Gm. of saccharin are also present in each lozenge.
Trochisci Santonini	Troches of Santonin	Contain santonin, tragacanth, prepared cocoa and sugar, and vanillin as a flavoring.
Trochisci Santonini Compositi	Compound Troches of Santonin	Contain santonin, calomel, tragacanth, cocoa and sugar, and vanillin as a flavoring.
Trochisci Sulphuris et Potassii Bitartratis	Troches of Sulphur and Potassium Bitartrate	Contain washed sulphur, potassium bitartrate, tragacanth and sugar, and oil of orange as a flavoring.
Trochisci Ulmi	Troches of Elm	Contain finely powdered elm bark, tragacanth and sugar, and methyl salicylate as a flavoring.

CHAPTER XXX.

COMPRESSED TABLETS AND TABLET TRITURATES.

COMPRESSED TABLETS.

THIS class of remedies, allied to lozenges, under the name "compressed pills," was introduced into England over sixty years ago, and some years later into this country. The former name, although in a measure erroneously applied, because pills are understood to be made from a previously prepared plastic pill mass, is still used by one or two manufacturers. Compressed tablets are lenticular-shaped disks containing one or more medicinal agents, and are obtained by compressing the material in the form of a granular powder into suitable shape by means of specially constructed apparatus operated by hand, steam, gas, or electric power.

Compressed tablets, although greatly in favor among physicians, for many years left much to be desired, and it is doubtful whether their extended use was justified, since the firm compression rendered many of them slowly soluble, while those containing insoluble substances failed to break up in water or the fluids of the stomach, even after hours of contact, so that the action of such tablets was either very much retarded or altogether prevented. Of late years, however, great improvements have been made in this respect, and compressed tablets are now made in such form that they will disintegrate within a few seconds when placed in water. This rapid and complete disintegration is especially desirable for such insoluble substances as bismuth subnitrate, bismuth subgallate, calcined magnesia, quinine sulphate, and various combinations of these with other substances. Its achievement must be admitted to be a decided and valuable improvement, and the process by which it is done is quite simple. The admixture of dehydrated starch (powdered starch ordinarily containing about 14 per cent. of moisture) with the granulated mixture as it is being fed into the compressor is known to impart to the tablet its disintegrating property, the exact quantity of starch necessary varying with different combinations. It is possible that manufacturers employ other agents in addition to starch, with a view to increasing the rapidity of disintegration of the tablets; but if so, such additions are not made public, and the secret is strictly guarded; plain starch, however, has been found very efficient. In addition to this improvement, the ready portability of compressed tablets, their convenient dosage, and comparative tastelessness when swallowed, together with their stability when properly made and kept, have at the present day

increased their manufacture and use to an enormous extent. The fact that compressed tablets may be readily sugar-coated or chocolate-coated has also added much to their popularity. The variety of combinations of medicinal agents capable of being presented in this form is practically without limit. Nevertheless not all medicaments are suitable for preparation into compressed tablets. This is especially the case with very volatile or readily oxidizable substances, since in the necessary exposure of the material during its preparation for compression considerable loss by volatilization is likely to occur, as in the case of camphor, or the material is changed by oxidation, as in the case of phosphorus. For such substances a well made pill properly protected by a coating is to be preferred.

It is manifestly impossible to give complete working directions for the preparation of every possible combination of remedial agents in compressed tablets, and much must be left to the judgment of the operator as each case presents itself. The general principles underlying this branch of pharmaceutical manipulations, however, are elucidated here. The first object must be to obtain the material to be compressed in the condition of a fairly uniform granular powder, a No. 20 or No. 30 granule being the usual degree of fineness employed. Fine powders are not adapted for compression, since the air which they carry with them when fed into the die is confined in the interstices between the particles, and cannot escape upward or downward during compression between the closely fitting dies and punches, hence imperfect compression results; moreover, fine powders have a tendency to cake or pack closely, and therefore do not feed regularly into the die. They also have a greater tendency to adhere to the surfaces of the punches and the sides of the die than does the same material in a granular form.

When the tablet to be compressed is to contain a single medicinal substance, this can often be bought in a granular form from the wholesale dealer, as, for instance, potassium chlorate, potassium sodium, and ammonium iodides, bromides, and chlorides, potassium permanganate, sodium phosphate, zinc sulphate, etc. In such cases it is only necessary to reduce the commercial granular powder to a more uniform condition by passing it through a clean No. 20 iron sieve. No excipient whatever is necessary for these substances, although at times it may be necessary to subject the material to the action of dry, warm air for a short time, in order to free it from accidental moisture. When salts containing water of crystallization are to be compressed alone and require previous drying, care must be taken not to expel any of this water. Sometimes crystallized salts may be reduced to the proper granular condition by simply grinding them in a mill.

Greater difficulty is experienced and more care must be exercised when two or more substances, either all medicinal or part medicinal and part diluent or excipient, are to be mixed and granulated. In

such cases all ingredients should be in a form of a fine powder. If potent remedies are to be incorporated, they should be thoroughly triturated either with the diluent or with the other ingredients, and the mixture should then be passed through a No. 80 bolting-cloth sieve, and again well mixed after sifting. The mixture is then moistened with whatever fluid or mixture of fluids the medicinal constituents or the diluents or excipients may dictate. The moistening fluid may be water, alcohol, a mixture of alcohol and water in various proportions, or aqueous solutions of glucose of different strengths. It is stated that sometimes a weak solution of gelatin has been used with good results, but glycerin should never be used, since it does not dry out and has a tendency to render the granules sluggish, when feeding into the die. The fluid should be carefully and uniformly distributed through the entire mass, and in most instances only a sufficient quantity should be used to produce a well moistened powder. This is then pressed through a No. 12 or No. 16 brass, iron, or tinned iron-wire sieve. The choice of the size and kind of sieve will depend on the physical and chemical properties of the material being operated upon, and these properties may render it necessary to omit the passing of the moist powder through a sieve altogether. This is the case when any constituent of the mixture is likely to be affected by the metallic surface of the sieve, as, for instance, the various mercurials, salicylates, etc. Sometimes also the components when moistened form too tough a mass to permit its being forced through a sieve. In such cases the material is dried out immediately after having been moistened, and is then ground in a mill or a mortar to the proper granular condition. The moistened powder which has been forced through a sieve is spread on glass plates or sized paper, and dried by exposure to either ordinary or warmed air. The physical and chemical properties of the substance will again dictate the conditions under which this drying should be conducted. Readily fusible (salol) or volatile (camphor, benzoic acid, essential oils, etc.) substances should be dried in the cold. When small quantities of volatile substances, as, for instance, flavoring oils, etc., are to be incorporated, they may be omitted from the mass and subsequently sprayed over the dried granules after having previously been dissolved in a little alcohol or ether. The granules should then again be carefully mixed. Most substances permit drying by means of circulating warm air, and all such as are readily affected by light should be carefully protected during drying. The dried granules are now forced through a No. 20 or No. 30 sieve. If during this operation much fine powder has been produced, it may be necessary to separate the same by means of a fine sieve and to regranulate it.

To overcome the tedious operation of granulating the material by hand, special machines have been designed for use in large laboratories where often from 50 to 100 pounds of granules are handled at one time. In some cases it will suffice to simply dampen the powder, and for this purpose the granulating mixer shown in Fig. 271 answers well, the

granulating fluid being allowed to drip onto the powder while it is constantly stirred; the mixture does not become wet enough to form a mass and yet granulation is readily effected. For the purpose of forming a mass and granulating the same by forcing it through a sieve of proper size, the machine shown in Fig. 272 is to be preferred.

Sometimes it is necessary to add to the granular powder a lubricant, preferably the best quality of liquid petrolatum, in order to enable the tablet to be more readily expelled from the die. Usually about 1 fluidrachm of liquid petrolatum to 1 pound of granules is sufficient, it being dissolved in about an equal volume of ether and sprayed over the granules. In order to prevent the material from adhering to the punches, the granules may be dusted with a little finely powdered talcum or lycopodium, about $\frac{1}{4}$ ounce of the former or $\frac{1}{8}$ ounce of the latter to a pound. When tablets are to be used for preparing clear

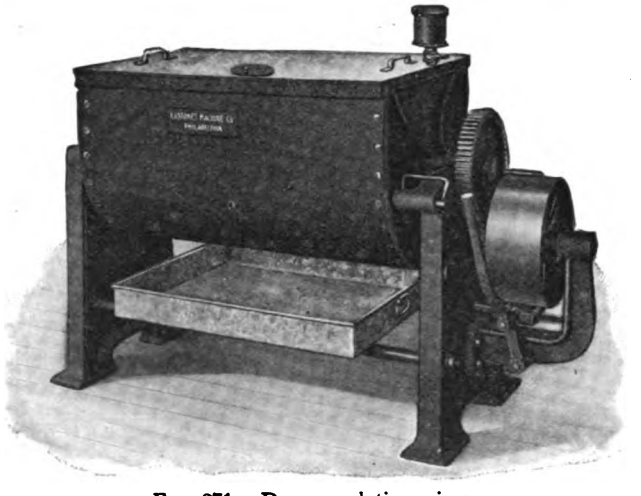


FIG. 271.—Dry granulating mixer.

solutions, a little boric acid may be used in place of the talcum or lycopodium, provided the acid be not incompatible with the constituents of the tablet. Care must be taken not to crush the granules while the lubricants are being added.

When substances possessing no inherent adhesiveness are to be granulated, they require the addition of an excipient, such as acacia, sugar, tragacanth, or glucose, the first three in the form of fine powder, the latter in solution. Of all such substances, charcoal probably requires the largest proportion of excipients, from 5 to 10 per cent. of gum together with 15 or 20 per cent. of sugar or glucose being necessary; water is used as the moistening agent, and the mass must be well worked.

Tablets containing such sparingly soluble substances as acetanilid, phenacetin, salol, sulphonal, etc., are improved by the addition of a little starch.

Whenever tinctures or fluidextracts are to be administered in compressed tablet form, they are preferably evaporated with moderate heat over a waterbath to a syrupy consistence before they are mixed with the other ingredients; if no other diluent powder has been prescribed, the syrupy liquid may be incorporated with a mixture of finely powdered starch and sugar for the purpose of granulation. Solid extracts may be used either in the form of a vacuum-dried fine powder or the pilular extract may be softened with a little alcohol,

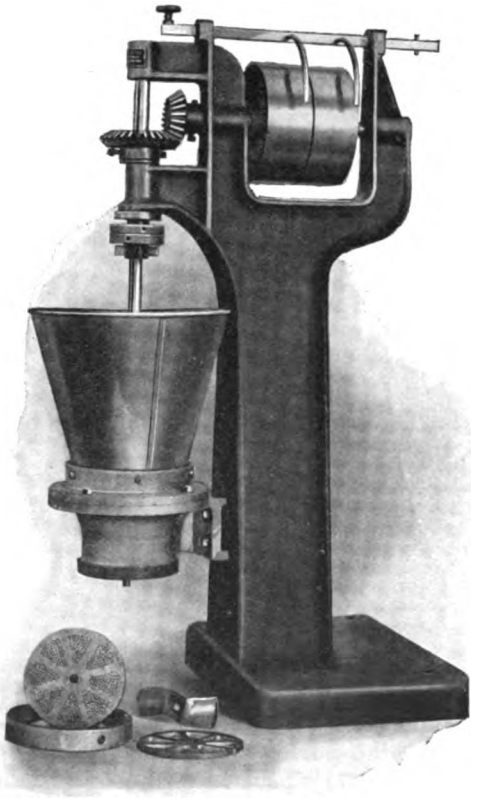


FIG. 272.—Improved wet granulating machine.

alcohol and water, or water, as may be necessary. The softened extract is then incorporated with the diluent or other ingredients, which may necessitate working the mixture into a perfectly uniform pill mass, to be then broken into small pieces and dried, and finally ground to the proper granular condition.

If tablets, upon solution, are designed to yield effervescent draughts, they may be made by first preparing the corresponding granular effervescent salt and compressing this, or the ingredients upon which

the effervescence depends may be granulated separately in granules of the same size and then thoroughly dried and mixed just before compression. Thus, if effervescent tablets of lithium citrate or carbonate are wanted, the lithium salt could be granulated with the sodium bicarbonate, while the tartaric acid may be granulated separately with alcohol or water. All effervescent tablets must be carefully protected against moisture in air-tight bottles.

The preparation of compressed tablets in small quantities may be conveniently accomplished at the dispensing counter, and various combinations readily furnished on extemporaneous prescriptions. The finely powdered ingredients, having been intimately mixed and properly dampened, preferably with syrup, may be quickly passed through a No. 20 or No. 30 sieve, and the granules readily dried by rapidly rotating them on a sheet of smooth paper placed in a sieve or on a perforated tray over a stove or other heated surface; as soon as dry the granules should be weighed and divided into the requisite number of parts, which will then be ready for compression.

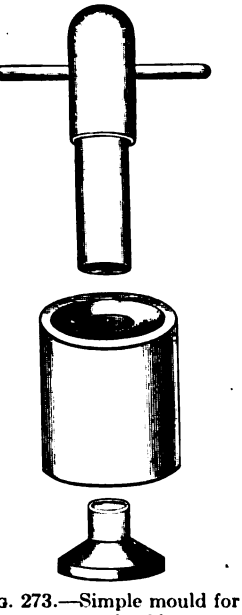


FIG. 273.—Simple mould for compressed tablets.

Different styles of compressors have been designed at various times to suit the purposes of dispensing pharmacists (see Figs. 273 and 274). They are all fed on the same principle, and the mode of operating them differs but slightly. The cylinder, base, and piston are usually made of hardened steel, nickel-plated; the base, which is made to project somewhat into the cylinder, as shown in Fig. 273, having been adjusted, the granular substance is carefully fed into the cylinder from a piece of stiff paper, the piston is inserted over the granules, and compression effected either by a sharp blow from a wooden mallet, or by means of a lever, as shown in Fig. 274.

The Smedley Compressor was constructed on the above principle and did good service for many years, but it is no longer manufactured. The tablet machine made by the Whitall-Tatum Co., of Philadelphia (see Fig. 274), is well adapted for use at the dispensing counter. The depth of the mould is regulated by means of a screw, so that after weighing out the powder for one tablet and adjusting the mould so that it will just contain the powder before compressing, the tablets will be made of uniform weight and thickness by simply filling the mould to the top for each tablet.

When the lever is thrown back, the lower die is automatically raised, discharging the tablet. It then recedes to its former position

and the mould is ready for refilling. Each machine is furnished with two sets of moulds and dies, making tablets respectively of $\frac{5}{16}$ and $\frac{6}{16}$ inch diameter, and of thickness as required.

The greater the pressure applied, the firmer will be the compression, but at the same time the slower will be the disintegration of some compressed tablets; hence only sufficient pressure should be used to cause the particles to cohere properly without crumbling when handled or breaking if allowed to fall.

When too much pressure has been applied some tablets "chip" or "cap," a portion of or the entire upper convex layer showing a tendency to split off. This difficulty may sometimes be remedied

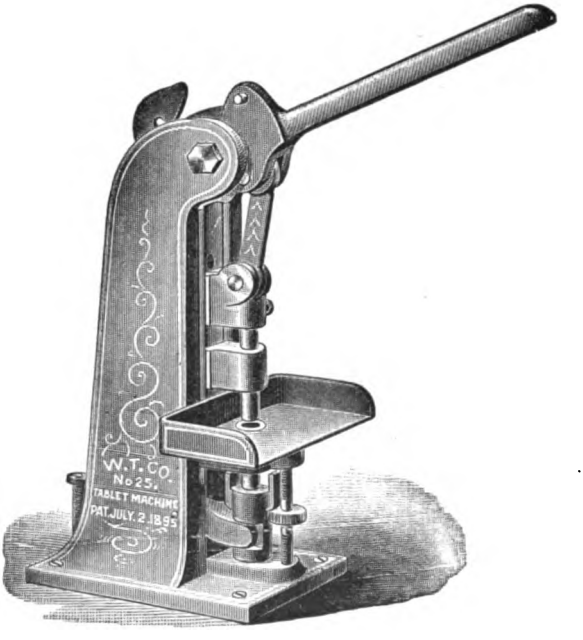


FIG. 274.—Tablet compressor.

by reducing the pressure in the operation, or it may be overcome by adding a little water to the granules, about 1 or 2 drachms to the pound, by means of an atomizer.

If at any time a compressed tablet should become fixed in the cylinder or in the concave depression of the piston, or possibly, if fine powder, having been inadvertently used, some of it should have been forced between the piston and the sides of the cylinder, and thus have fastened the piston, warm water alone should be used to relieve the trouble; never should a sharp instrument be employed to loosen the adhering material, as this would be likely to produce rough surfaces or edges, thereby rendering the compressor unfit for use.

The Eureka tablet machine (Fig. 275) and the Freck tablet compressor (Fig. 276) insure greater uniformity in thickness of the tablets than the apparatus above described. Both machines are provided with an automatic feeding attachment, and hence the tablets can be compressed more rapidly than in other hand machines. In both cases the depth of the mould is regulated by means of a screw, so that after weighing out the material for one tablet and adjusting the mould so it will just hold the same when filled to the top, the tablets are sure to be of uniform weight when compressed.

In the Eureka machine the material is placed in the shoe-shaped hopper shown in the figure, the movement of which is controlled by the large fly-wheel, and which also simultaneously controls the motion

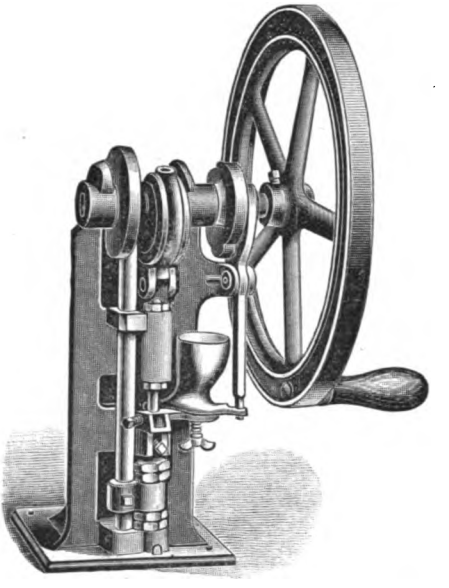


FIG. 275.—The Eureka tablet machine.

of the upper and lower punches. The feeding of the mould is effected from the shoe, which as the wheel is revolved moves forward sidewise with a jerky motion, so that when over the mould the material readily drops into the latter. The further motion of the fly-wheel causes the shoe to return to its original position and at the same time the upper punch descends and compresses the material in the mould, and as the shoe again advances to refill the mould the lower punch rises to push the tablet above the mouth of the mould, whence it is thrown forward into a receptacle by the shoe passing over the mould. The machine is easily understood and readily adjusted, and with a little practice can be made to compress 100 tablets or more a minute.

The Freck tablet compressor, made by the Wm. Freck Co., of

Chicago, is apparently one of the best ever made for compressing a small number of tablets at the dispensing counter or even a hundred or more, inasmuch as the pressure can be regulated, and thus uniformity in thickness and hardness of the tablets be insured. It occupies a space of 5½ by 8 inches, and the lever is of such length that each pound of pressure upon it is multiplied to 12 pounds on the die. Its construction and mode of operation are best explained by means of the letters shown in the figure: *A* is the funnel-shaped feeder into which the granulated material is put and which fills the dies; *B* is a set-screw which holds the upper punch; *C* is a set-screw which holds the lower punch; *D* is a set-screw which prevents the regulator from moving; *E* is the regulator for adjusting the capacity of the dies and

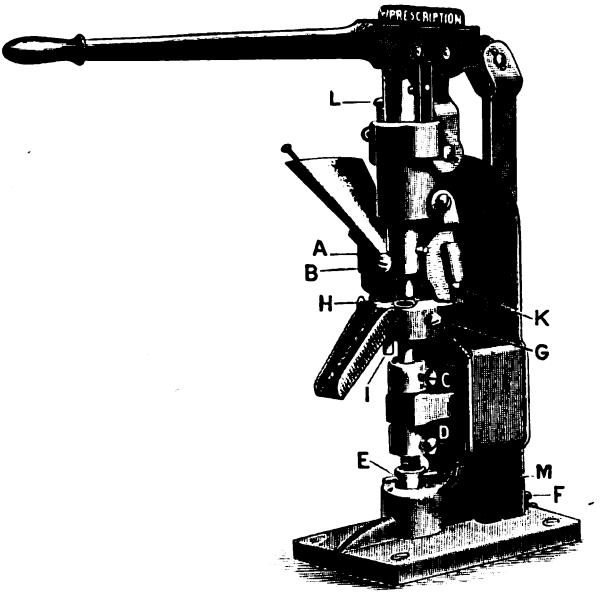


FIG. 276.—The Freck tablet compressor.

consequently the weight of the tablet; *F* is an adjusting screw for stopping the lower punch even with the surface of the die; *G* is a set-screw which holds the die; *H* is a set-screw for the pin *I*, which swings the feeder; *K* is the point which holds the feeder to the surface of the machine, and automatically throws the feeder out of the way when the upper punch is descending; *L* is a screw by means of which the lever-handle may be stopped at a certain distance, so as to give uniform thickness and hardness to the tablets; *M* is a hole into which a pin is inserted when the handle is raised to its highest point to put it out of gear. As in the Eureka machine, the tablets when compressed are brought above the mouth of the die by the lower punch ascending, and are then removed by the feeder and slide down the chute into a receptacle.

For manufacturing compressed tablets on a large scale, special machinery has been constructed to be operated by steam power. These machines can be so adjusted that a definite quantity of material will be automatically fed into the mould; therefore, as the pressure applied is uniform, the resulting tablets must be of even weight and

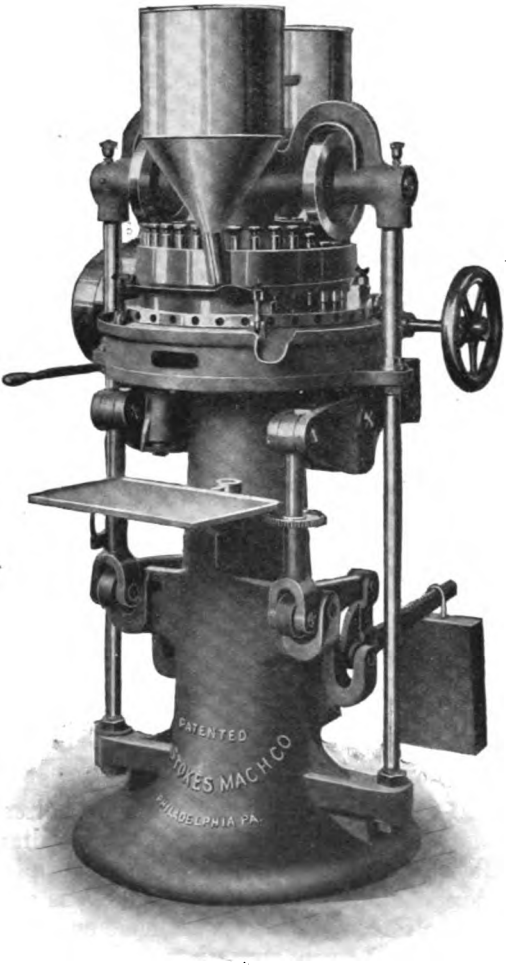


FIG. 277.—Clark rotary tablet machine "B–B."

thickness. Improvements are constantly being made in the various compressors used by large manufacturers; the Clark rotary tablet machine, shown in Fig. 277, is perhaps the most perfect tablet compressor made. It is constructed on a different principle from other tablet machines, is absolutely noiseless, and capable of delivering 1500 tablets a minute. This machine will make any size of tablet

from $\frac{1}{8}$ to $\frac{1}{2}$ inch in diameter, the tablets being compressed on both sides of the machine and delivered into one receptacle in front; the punches are not fastened, and can be lifted out by the fingers instantly. It is provided with two large hoppers for feeding the granulated material to the dies and excessive pressure is automatically released by the safety weight attached below.

In all automatic tablet machines the adjustment of the supply of material to the dies must be made tentatively. The first adjustment is merely approximate, and after the weight of the first tablet thus compressed has been determined, the capacity of the die is increased or decreased, as may be necessary. The proper adjustment having been made, the shoe can supply only as much material as the die will hold, hence the automatic supply must be uniform and exact.

In order to insure a well shaped tablet, the diameter of the die must be selected in proportion to the weight of each tablet. Thus for material of average density tablets weighing 1 grain may be made with dies $\frac{7}{32}$ of an inch in diameter; $1\frac{1}{2}$ grains will require a $\frac{1}{4}$ inch die; 2 grains, a $\frac{9}{32}$ inch die; $2\frac{1}{2}$ or 3 grains, a $\frac{5}{16}$ inch die; $3\frac{1}{2}$ or 4 grains, a $\frac{11}{32}$ inch die; $4\frac{1}{2}$ to 5 grains, a $\frac{3}{8}$ inch die; 6 or $6\frac{1}{2}$ grains, a $\frac{13}{32}$ inch die; 7 or 8 grains, a $\frac{7}{16}$ inch die; 10 grains, a $\frac{1}{2}$ inch die; 20 grains, a $\frac{5}{8}$ inch die, and so on. If the material to be compressed be of high specific gravity, as, for instance, calomel, bismuth subnitrate, etc., a die of smaller diameter must be chosen for the weights mentioned above. Compressed lozenges, which are merely large compressed tablets, with the usual constituents of lozenges, however, are made with $\frac{1}{2}$ to $\frac{5}{8}$ inch dies according to the weight of the lozenge. In order to insure good results, the sides of the bore of the die and the concave surfaces and sides of the punches must be kept highly polished. The edges of the punches must be kept sharp and perfect, otherwise there will be an irregularity on the surface of the tablet. After the dies have been used they should be carefully washed and dried and smeared with a little vaselin, to prevent rusting; they should then be stored in a dry place.

Official Tablets.—The U. S. Pharmacopœia recognizes but one kind of tablet, officially designated as Toxitabellæ Hydrargyri Chloridi Corrosivi or Poison Tablets of Corrosive Mercuric Chloride, also known as Bichloride Tablets. No official directions are given for the preparation of these tablets, but they are made on a large scale either by compression of a previously prepared mixture of mercuric chloride and sodium chloride in granular form, or the mixed material is made into a somewhat stiff paste, after the manner of preparing a mass for tablet triturates, and is then moulded in a suitable apparatus.

The tablets are required to be of angular, not discoid, shape, each having the word "POISON" and the skull and cross-bones design distinctly stamped on it. They must contain about 0.5 Gm. of corrosive mercuric chloride and are to be colored blue, preferably with sodium indigotindisulphonate, and dispensed in glass-stoppered containers

bearing a red label on which appear the word "POISON" and a statement indicating that the tablets contain the required amount of corrosive mercuric chloride.

The German Pharmacopœia recognizes the same combination of mercuric chloride and sodium chloride, but in cylindrical form instead of angular, and colored red with some coal-tar dye.

On account of the very dangerous character of mercuric chloride tablets, they should never be sold indiscriminately to the public, but only on physicians' prescriptions. The careless sale and use of these tablets has led to many accidents and suicides.

TABLET TRITURATES.

This class of preparations was introduced, in 1878, by Dr. R. M. Fuller, of New York, no doubt, with a view of administering small quantities of potent remedies in convenient and readily soluble form. Since then some manufacturing firms have made strong efforts to induce physicians to resort to this method of medication for the purposes of office dispensing. That the growth of homœopathic patronage has largely aided the introduction and use of tablet triturates cannot be denied.

Tablet triturates are made by triturating the active ingredient with either plain sugar of milk or a mixture of sugar of milk and ordinary or cane sugar (usually in the proportion of 4 or 5 parts of the former to 1 part of the latter), and then moistening the mixed powders with sufficient alcohol, alcohol and water, alcohol and syrup, or water alone, to thoroughly dampen the same without making the mixture pasty, and finally pressing the damp powder into tablets in appropriate moulds. The composition of the liquid excipient to be employed will vary greatly according to the diluent used, the nature of the medicinal ingredients operated upon, and also the quantity to be present in each tablet, the aim being to produce a partial softness in the mixture which will enable the particles to cohere when the damp powder is compressed between the fingers. When simply milk sugar is used as a diluent, water alone will answer as the excipient in most cases; but when a mixture of milk sugar and cane sugar is used, a strongly alcoholic liquid excipient is necessary, on account of the ready solubility of cane sugar in water, the proportion of alcohol being increased as the quantity of cane sugar is augmented. For most operations at the dispensing counter, where no special facilities for rapid drying are at hand, a mixture of 5 parts of milk sugar and 1 part of cane sugar, together with an excipient composed of 5 volumes of alcohol and 1 volume of water, will perhaps prove most desirable, as the greater volatility of the alcohol insures more rapid drying of the tablets.

It is essential that the sugar be in very fine powder, in order to yield a smooth paste and perfect tablets; and if the mixture be passed

through a No. 120 sieve before making the paste, the results will be all the better. A few cases will occur in which sugar and other organic matter are inadmissible as a diluent, owing to chemical changes likely to occur; as, for instance, potassium permanganate, silver nitrate, etc.; finely powdered kaolin, or pipe-clay, should then be used with water as an excipient.

Tinctures and fluidextracts, unless strongly alcoholic, are made into tablet triturates with more or less difficulty, according to the amount of fluid to be represented in each tablet, and may require evaporation to dryness with a portion of the sugar, so as to be subsequently reduced to fine powder, prior to converting into a suitable paste. The presence of glycerin, especially if in large proportion, is objectionable, since it keeps the extractive matter soft and prevents proper drying of the tablets. In some instances it will suffice to concentrate the fluid by evaporation and use it, in place of an excipient, for moistening the mixed powders; but this plan can only be followed when the proportion of fluid ordered is small or when it has been made with a strongly alcoholic menstruum. Solid extracts can be introduced only in small proportions, and may then be incorporated as indicated under Compressed Tablets; more than one-fourth or one-third of the total weight of the tablet triturate is not advisable. In such cases, and also in the case of tablets to contain various amounts of tinctures or fluidextracts made with hydro-alcoholic menstrua, a mixture of milk sugar and starch in varying proportions will be found the best diluent. Such mixtures are often difficult to form into smooth tablets, and the tablets when dried are often very hard. Tablet triturates containing $\frac{1}{4}$ grain or more of solid extract or 1 minim or more of hydro-alcoholic fluidextract can be made more friable by using a mixture of milk sugar and starch as diluent and granulating the well mixed mass as directed under Compressed Tablets, and subsequently compressing the dry granules by means of a compressing apparatus into shape similar to that of tablet triturates. Enough diluent should be used to make the finished tablet weigh about $1\frac{1}{2}$ grains each. The pressure is readily regulated so as to produce a friable tablet. The punches used for this purpose should have flat surfaces, to insure the customary shape and appearance of tablet triturates, although concave punches will yield tablets equally friable. Substances of a volatile or deliquescent character, or such as are readily oxidized upon exposure to air, are wholly unfit for tablet triturates; hence camphor, creosote, calcium sulphide, arsenic iodide and bromide, potassium citrate, scale salts of iron, phosphorus, and the like, should never be dispensed in this form.

Moulds for Tablet Triturates.—Until recently all tablet triturates had to be moulded by hand, the apparatus employed, whether for small quantities at the dispensing counter or in the manufacture of tens of thousands in the laboratory, consisting of two plates, as shown in Fig. 278. The plates, although sometimes constructed of metal

are preferably made of hard rubber, the upper one being perforated and the lower provided with a corresponding number of pegs, which fit accurately into the perforations of the upper plate. In order to insure the exact position of the pegs when the upper plate is brought down over them, two guide pins are fastened to the lower plate, one near each side; these extend above the pegs and enter two corresponding holes in the upper plate. As a rule the plate moulds are made to prepare 50 or 100 tablet triturates at one time, although some are provided with 200 or more perforations, and a few with only 25. The perforations in plates of the standard size adopted for tablet triturates measure $\frac{7}{32}$ of an inch in diameter, and $\frac{1}{8}$ of an inch in depth. In a few instances moulds are used with perforations $\frac{9}{32}$ of an inch in diameter and $\frac{1}{8}$ of an inch in depth; larger tablets are now generally made by compression, since the same weight of material can by this method usually be obtained in smaller bulk.

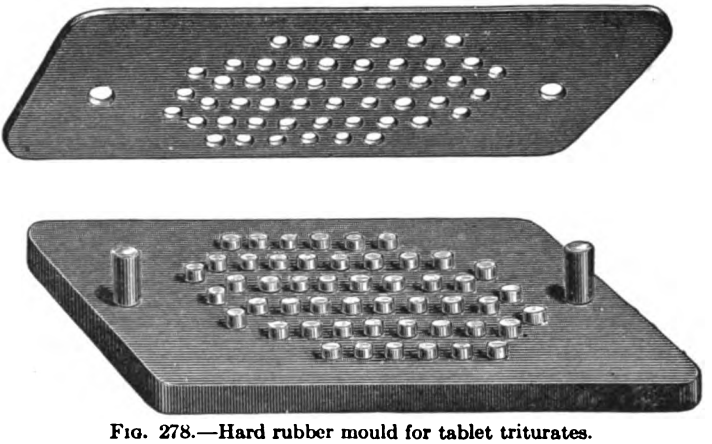


FIG. 278.—Hard rubber mould for tablet triturates.

Hard rubber moulds require considerable care in cleaning and in storing them when not in use, in order to preserve the original perfect shape. They should never be exposed to heat, either by using hot water for washing or dry heat for drying them, as the moulds are thereby warped and the accurate adjustment of the pegs and perforations is destroyed; when thus warped, the moulds can only be used with great difficulty, and soon becomes worthless. A narrow, stiff paint brush will be found very serviceable in cleaning the moulds, and water at the ordinary temperature should be used for washing the plates; sometimes alcohol, or even acids, may be necessary to remove material tenaciously adhering to the moulds, but never should a sharp instrument be used in the perforations or on the pegs, as the smooth surfaces are likely to be scratched thereby. After the plates have been carefully cleansed and rinsed with cold water they should be dried with a soft towel, the water remaining between the pegs

being readily shaken out; when dry, the perforated plate should be placed in proper position on the peg-plate, and the whole laid aside on a level, solid, surface, away from heat.

Method of Moulding Tablet Triturates.—When a properly dampened powder mixture has been prepared, the perforated plate is placed upon a level surface, preferably a thick glass plate, and, by means of a horn spatula of the shape shown in Fig. 279, the mass is forced into the holes so as to fill these completely, any excess of material being removed with the spatula; the plate is then reversed and if necessary more of the mass is forced into the holes until they are completely filled and both sides present a smooth, solid surface. The operation is best explained as follows: The operator grasps the spatula in such a manner that the forefinger rests on the flat surface near the acute angle of the diagonal edge, with the middle finger resting near the obtuse angle of the same edge; the thumb rests against the long side, and the third and little fingers against and slightly around the short side of the spatula. The mass having been placed on the mould under the spatula, the latter is drawn with pressure over the mould diagonally toward the operator. After the required number of holes have been

FIG. 279.—Horn spatula.

filled, the upper plate is carefully brought down over the lower one with the marks or numbers at the end of the two corresponding, and by the aid of the guide pins the pegs are pressed into the corresponding holes and the tablets thus forced out, remaining on the ends of the pegs; after a few moments they may be removed, either by inclining and tapping the plate or by carefully brushing them into a suitable receptacle, preferably a bolting-cloth sieve. The tablets should then be dried either by exposure to the ordinary room temperature, protecting them from dust, in closets supplied with circulating warm air, or in small quantities on a perforated tray near a stove or register, as the nature of the medicinal ingredients may permit. By means of hard rubber moulds holding 100 tablets each, experienced operators average from 6000 to 8000 tablet triturates per hour, unless the material be especially difficult to manipulate.

The weight of different kinds of tablet triturates made with moulds of the standard size mentioned above will vary considerably according to the density of the mass being manipulated. Thus tablets containing $\frac{1}{4}$ grain of morphine sulphate each, will weigh about 1.2 grains; tablets containing $\frac{1}{4}$ grain of calomel will weigh about 1.4 grains; and tablets containing 1 grain of calomel will weigh from 1.9 to 2 grains each;

while the size of all of these tablets will be the same. The weight of the tablets will also be considerably influenced by the pressure upon the spatula exerted by each individual operator during the process of moulding, which varies with nearly every person, and hence in large manufacturing establishments operators are kept at work on certain lines of tablet triturates with which they have become familiar so as to insure uniformity in weight. The weight of a certain tablet having been ascertained, a memorandum should be made of the details regarding combination, diluent, and excipient, for future reference.

Every formula for new tablet triturates must be determined tentatively in order to ascertain the exact amount of sugar of milk or other diluent required. The simplest plan is to weigh off enough of the active ingredients to make a given number of tablets (say 25 or 50); mix this with a quantity of diluent known to be insufficient, moisten with the necessary excipient, and press the mass into the holes of the plate intended to be used. Then moisten more of the same diluent with the excipient, and with this paste fill the holes remaining unfilled from the first operation; smooth off both sides of the tablets, place on the ejecting pegs and force the tablets out. For larger operations the tablets should then be thoroughly dried and weighed, the weight of the dry tablets less the weight of active ingredients used representing the weight of the diluent required to make the given number of tablets. In small operations, particularly those of the dispensing counter, the drying may be omitted, and, instead, an extra number of tablets (4 or 5) made out of the plain diluent, added to the number first obtained, before the whole is thoroughly mixed in a mortar; this extra material is necessary because the first tablets, when worked up again in the mortar, generally form a more compact mass, and hence would prove insufficient for refilling the required number of perforations. The porous nature of most tablet triturates and the very fine state of division of the ingredients render it essential that the tablets be carefully kept in dry, tightly stoppered amber-colored vials, which protect them perfectly against the air, moisture, and the effects of the light. They should be stored in a cool and dry place. Small amber-colored homœopathic vials are likewise the best receptacles for dispensing these tablets. Tablet triturates containing substances readily affected by air or light are often made into compressed lenticular-shaped disks and subsequently coated with sugar or chocolate.

The automatic tablet triturate machine (see Fig. 280) made by the Arthur Colton Co., of Detroit, Mich., is a very ingenious device, and, according to the claims of the company, should prove of great value to large manufacturing establishments. It is said to be capable of producing a million tablet triturates per day with the aid of but one operator. The prepared material having been placed in the hopper, passes through the funnel of the hopper to a feed plate below, in which are four holes of the same diameter as the mouth of the funnel. One

hole is filled at a time and then passes around to the mould plate; when in position the weighted pressure foot comes down and a spreader in the sole of the foot forces the material evenly and smoothly into the cavities of the lower plate, which then passes on to the next position, where it registers with a set of punches which eject the tablets onto a glass plate inlaid in the bed of the machine, from which they are pushed mechanically to a chute leading to a tray.

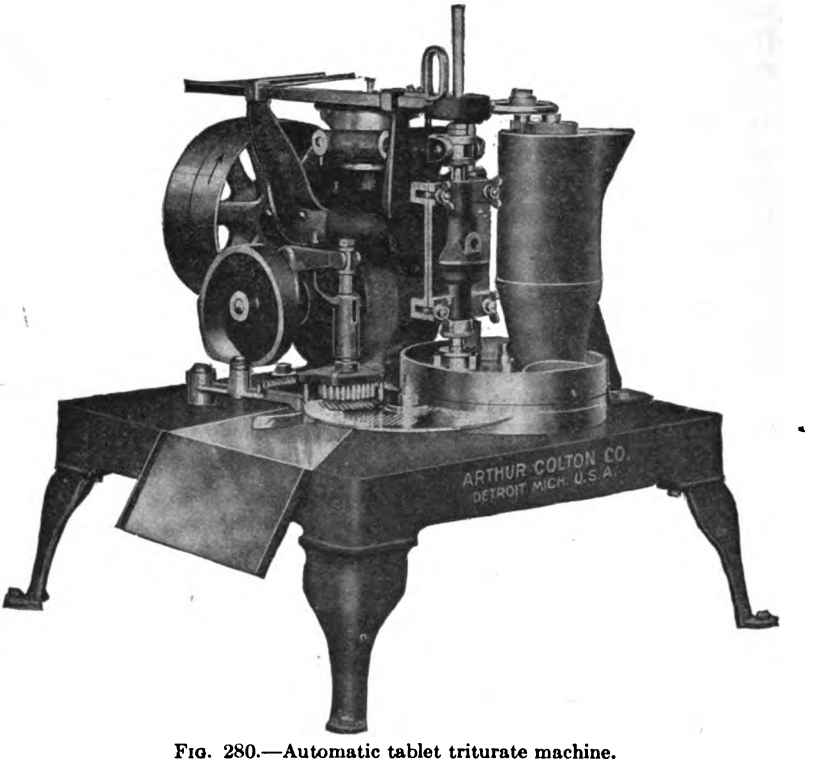


FIG. 280.—Automatic tablet triturate machine.

Tablet Saturates.—Tablet saturates differ from tablet triturates only in the manner of introducing the medicinal agents. They are made by first preparing plain sugar of milk tablets, in the moulds already described, and having placed the tablets, when dry, on a glass plate, the desired quantity of tincture, fluidextract, or solution is dropped upon each tablet individually from a pipette. A glass cover is then placed over the tablets and the fluid allowed to saturate them uniformly, after which they are dried in a current of warm air.

Hypodermic Tablets.—Hypodermic tablets are simply tablet triturates intended for the convenient preparation of solutions for subcutaneous injection. Since they contain definite quantities of the active agents, they are admirably adapted for physicians' use at

the bedside, and are very extensively employed. As a rule pure sugar of milk or pure cane sugar is used as the vehicle, although sodium sulphate has also been employed by some manufacturers. They are made in the hard rubber moulds already described, the perforations being usually $\frac{5}{32}$ inch in diameter and $\frac{1}{10}$ or $\frac{1}{8}$ inch in depth. This produces a tablet that can readily be dropped into the barrel of a hypodermic syringe, in which it is quickly dissolved upon addition of 10 or 15 minims of water and subsequent agitation.

Ampuls.[1]—While hypodermic tablets are very extensively used in this country, sterilized solutions put up in small glass vessels called ampuls seem to be preferred in Europe, and have also been introduced into hospitals and private practice here. A brief description of these ampuls and the method of filling them is deemed appropriate at this point, especially since several American firms are now putting them on the market.

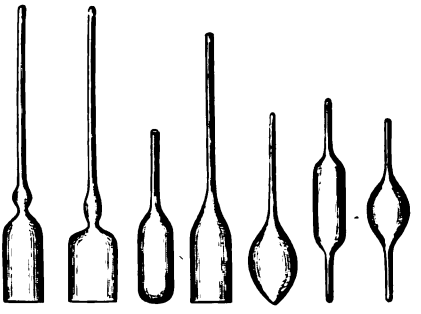


FIG. 281.—Ampuls.

The word ampul is derived from the French *ampoule*, and this from the Latin *ampula*, meaning a vase or flask. The name is applied to sealed glass vessels of varying capacity from $\frac{1}{2}$ milliliter (or cubic centimeter) to a liter, the latter being designed for large quantities of saline solution intended for intravenous injection. The form of ampuls varies as widely as the capacity, as may be seen in Figs. 281, 282, and 283. In this country and in Germany the bottle-shaped ampul is preferred, while the simple tube sealed at both ends is more popular in France and Italy.

Owing to the presence of soluble alkali in ordinary glass and its effect on certain solutions, especially of alkaloidal salts, neutral glass, such as Jena Normal 16 III, is preferred for the manufacture of ampuls, especially if they are to be used for solutions sensitive to alkali. For solutions liable to be affected by light, such as those of apomorphine hydrochloride, of ferric salts, of the salts of physostigmine, etc., amber-colored ampuls should always be used.

[1] Fuller information in regard to ampuls may be found in a paper by C. A. Mayo in Proc. A. Ph. A., 1909, p. 1106, from which this abstract was made.

Ampuls may be filled by gravity flow, by pressure, or by vacuum suction. For small operations, the gravity flow or the pressure method is preferable, by means of which one ampul is filled at a time; either method is well adapted for dispensing work. The liquid may be introduced from a glass pipette drawn out to a fine point of such length as to be readily inserted into the ampul, or a burette may be provided by suitable means with an aspirating needle or a capillary tube,

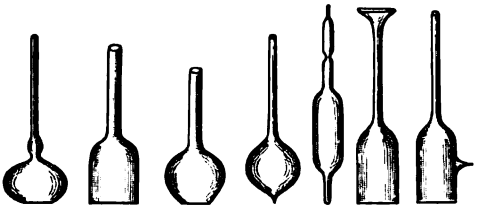


FIG. 282.—Ampuls.

and the flow of the liquid then regulated through the stop-cock of the burette; the latter method will be found the most convenient and expeditious. Finally the tips of the ampuls are sealed by fusing in the flame of a Bunsen burner.

In large manufacturing establishments where hundreds of ampuls are to be filled simultaneously the vacuum process is usually employed as follows: The ampuls having been placed neck downward in the solution contained in a shallow dish, the whole is placed in a suitable

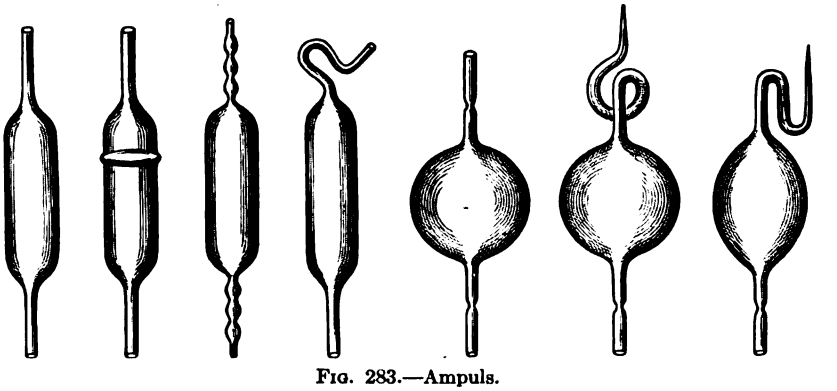


FIG. 283.—Ampuls.

apparatus, such as a vacuum desiccator, as shown in Fig. 284, No. 1; upon applying the vacuum, air is drawn out of the ampuls, and upon its release the solution is forced into the ampuls to take the place of the exhausted air, as shown in Fig. 281, No. 2, the ampuls being incompletely filled, as in the case of bottles, since only a partial vacuum is used. The ampuls are now reversed, and the vacuum is reapplied, whereby the liquid is drawn out of the capillary necks, as shown in Fig. 281, No. 3, after which they are ready for sealing.

Too much stress cannot be laid on the necessity for complete sterilization of the liquid contents of the ampuls; some manufacturers filter the solution through sterile porcelain filters and carefully examine the filtrate before it is filled into ampuls, while others sterilize the

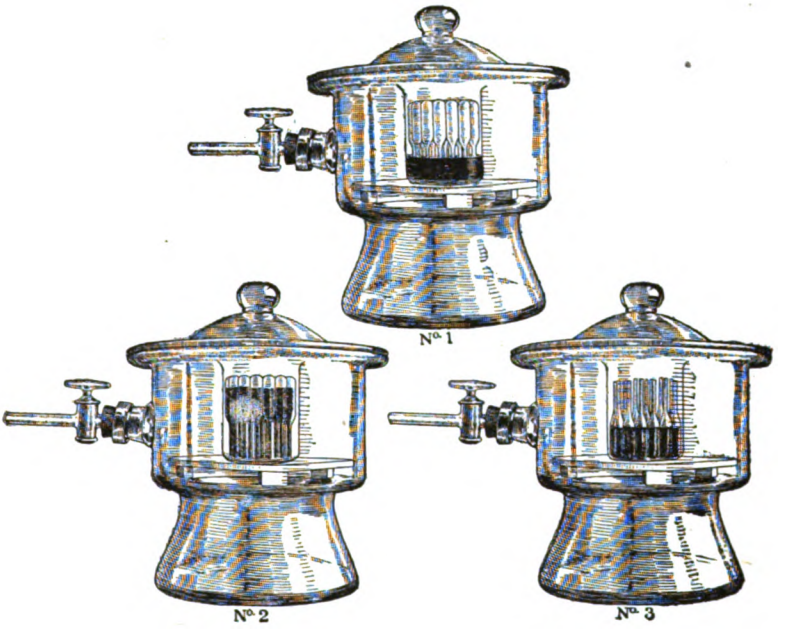


FIG. 284.—Showing the vacuum method of filling ampuls.

filled and sealed ampuls in a steam sterilizer; as already explained on page 140, some drugs are liable to decomposition by exposure to the temperature of boiling water, and in such cases intermittent sterilization at 60° C. (140° F.) for one-half hour at intervals of 24 hours for three or four consecutive days must be resorted to. The addition of ½ per cent. of phenol has also been recommended, which would prevent the germination of spores left in the solution, and does not seem to be objectionable from a therapeutic point of view.

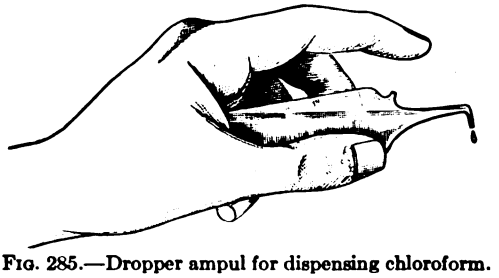


FIG. 285.—Dropper ampul for dispensing chloroform.

In Fig. 285 is shown a dropper ampul capable of holding 30 mils. (or Cc.) of chloroform; it was introduced by Parke, Davis & Co., of Detroit, Mich., for use in producing anesthesia. The well known tubes filled with concentrated nitrous ether or with ethyl chloride (kelene) may also be looked upon as special forms of ampuls.

CHAPTER XXXI.

POWDERS.

In addition to what has already been said about pulverization, in the chapter on Mechanical Subdivision of Drugs, there remains yet to be considered the administration of medicines in powder form, which, presenting certain advantages, is still largely employed by physicians. The powder form is a most convenient method of giving medicines in the case of very young children and persons who are unable to swallow pills, as well as where the fluid form is unavailable for any reason. It is true, many substances are not suited for administration in powder form, particularly bulky vegetable powders, deliquescent salts, and such as contain large quantities of water of crystallization, as sodium phosphate or sulphate, etc.; but while the fluid form of medicine is probably to be preferred in the majority of cases, the bitter or nauseous taste of some substances becomes more marked in solution than in the dry state. Among the substances best adapted for dispensing in powder form are insoluble chemicals, such as calomel, bismuth salts, mercury with chalk, some salts of the alkaloids, and vegetable drugs given in small doses, such as ipecac, opium, and catechu. Physicians frequently direct their patients to dissolve or mix the powder in water, and in such cases the powder form is preferred on account of convenience or for reasons of economy.

Fig. 286.—Porcelain powder mortar (sectional view).

Powders, as a rule, are composed of two or more substances; to insure an intimate and uniform mixture they must be triturated in a mortar, preferably made of porcelain, of the shape shown in Fig. 286, this style presenting a sufficient broad surface at the base, while its curved sides prevent the ejection of material during trituration. It is assumed that in the majority of cases the individual ingredients are already in the state of very fine powder, and therefore only require thorough mixing, which is best accomplished by trituration with light pressure only, so as to avoid caking and sticking to the sides of the mortar; the contents of the vessel should also occasionally be scraped from the pestle and sides of the mortar if necessary, as this aids more perfect admixture. Whenever substances which are themselves in a coarsely powdered or granular condition are ordered in a powdered mixture, they must be reduced to a very fine powder by themselves, no attempt being made to reduce them in the mixture.

A few general rules will serve for guidance in the preparation of mixed powders. Whenever sugar is one of the ingredients it should be of the kind known as bolted or lozenge sugar. When small quantities of potent or other substances are to be dispensed in powders, they should first be well triturated with a portion of the diluent, and finally incorporated with the remainder of the more bulky powders; or, if no diluent has been ordered, they should be triturated with a small quantity of sugar of milk, to insure their more uniform distribution in the mixture. The proper plan is to place about 5 grains of sugar of milk in the mortar, add the active ingredient, and then triturate thoroughly, as, by this means, more accurate subdivision is effected, and none of the active material is likely to adhere to the sides of the mortar. Soft extracts and essential oils must be treated in the same manner.

Whenever physicians prescribe quantities which cannot be weighed conveniently, such as $\frac{1}{6}$, $\frac{1}{10}$, $\frac{1}{24}$, or $\frac{1}{32}$ of a grain, and metric weights less than 10 milligrams, the plan of preparing a dilution of the substance with sugar of milk, by trituration, in such proportions that a weighable amount of the mixture shall represent the desired quantity of active ingredient, as indicated on page 394, should invariably be followed, as by this method accuracy of division is best obtained.

Certain substances of a crystalline structure—notably also those of a resinous character—have a tendency to become electrical by friction, particularly if pressure be employed; such bodies are said to be idioelectric, and must be triturated lightly, or, if pressure is necessary to reduce them to fine powder, they must be sprinkled with a little alcohol, whereby the trouble is obviated, or the powder, which adheres firmly to the mortar and pestle, and is prone to fly off in all directions if scraped with a spatula, must be set aside for awhile until the electric condition has disappeared. To this class belong common pine rosin, and the resins of guaiacum, jalap, and scammony, also quinine alkaloid, acetanilid, salol, phenacetin, and others. The removal of these in fine powder form from the mortar is attended with more or less difficulty unless previously slightly dampened.

When substances which differ materially in specific gravity are to be mixed in powder form—as, for instance, bismuth subnitrate with magnesia, sodium bicarbonate with charcoal, or zinc oxide with lycopodium—the best plan is to place the heavy substance in the mortar and incorporate the lighter body gradually by adding small portions at a time. Calcined magnesia and charcoal are also more readily mixed if the charcoal be gradually added to the magnesia with very light trituration; only in this manner can a powder of uniform appearance be obtained. Whenever large quantities of these powders are to be mixed, perfect blending may be achieved by shaking them together in a bottle for some time, and then passing the mixture repeatedly through a bolting-cloth sieve.

Since some substances when triturated together cause chemical

decomposition, attended in a few cases also with explosion, considerable care must be observed in mixing them; the offending ingredient should be reduced to fine powder by itself, and then cautiously mixed on paper with the other powders. Such conditions arise when potassium chlorate or permanganate is to be mixed with organic substances, as sugar, starch, tannin, gum arabic, and also sulphur and sulphides, or when lead acetate and zinc sulphate or borax and alum are triturated together.

Powders, whether simple or compound, intended for external application, by dusting or insufflation, must be passed through a fine bolting-cloth sieve, No. 120–No. 150, and should not then be triturated again before they are dispensed.

In the majority of cases medicines prescribed in powder form are dispensed in divided doses; although absolutely accurate division can only be obtained by weighing, this plan is rarely followed since practice will soon enable one to omit this tedious method. Usually the operator divides the mixed powder by the eye, either directly on the powder papers or by shaping the powder into a rectangle on a graduated tile, and dividing this into the requisite number of parts; an experienced dispenser is able to make quite accurate division from the mortar direct to the paper.

A convenient device for those who do not wish to entrust division of powders to the eye is the Diamond powder divider. This consists of a nickel-plated shallow metal trough, closed at one end and graduated on both sides; the powder having been introduced, a hard rubber plug is inserted at the open end and pushed up to the graduation indicating the number of divisions to be made. After levelling the surface of the powder by means of an accompanying flat bar, with handle attached exactly fitting into the trough, the rubber plug is removed and a quantity of the material, equivalent to one dose, as indicated by the divisions of the graduated sides, is transferred to paper by the aid of a spatula of the same width as the interior of the trough. The dimensions of the trough are 9 inches in length, 1 inch in width, and $\frac{3}{8}$ of an inch in depth.

For enclosing the divided doses of powder, either well calendered or parchment paper may be used; the latter is now preferred by many pharmacists, as it offers at the same time protection against the moisture of the air. Even those who use glazed white paper will find either parchment or waxed paper necessary for volatile or hygroscopic substances. Powder papers should be folded uniformly, hence it will be found advantageous to keep in stock a supply of the various sizes, already creased. This is readily done by folding the paper over a piece of stiff metal of suitable size, with rounded edges to prevent cutting, in such a manner that a narrow margin, about $\frac{1}{8}$ inch wide, is made on one of the long sides; the straight edge having been brought up against the crease of the margin, both ends are folded back to about the center of the piece of metal and firmly pressed down with a horn spatula. The two sides are now folded over the edges of the

metal plate and also firmly pressed, after which the creases are all opened and the plate is removed. Such creased powder papers not only insure absolute uniformity in size and shape, but have also been found very convenient in economizing time at the prescription counter. Some pharmacists prefer to fold each paper containing the powder over a powder box or specially constructed adjustable powder folder. The habit of flattening the powder within the paper by pressing it with a spatula is a bad one, and should never be followed, as it is likely to cause the powder to cake, and often interferes with its proper administration in liquids. To prevent any of the material from leaving the paper, one of sufficiently large size should be used, that the creases where the sides have been folded over may be pressed down with a spatula; this effectually prevents leakage.

A small number of powders in papers (two or three) are usually dispensed in an envelope, while the regular oblong powder boxes are used for larger numbers. When not divided into doses the powder is dispensed either in round paper boxes (never in paper, unless intended for use at one time) or in wide-mouth bottles; the latter method is necessary if the ingredients attract moisture or if very volatile substances are present, and will also be found convenient when travelling. When bottles are used, a piece of glazed paper should be inserted between the neck of the bottle and the cork, to prevent particles of the latter from falling into the powder.

While, as a rule, medicines in powder form are administered to the patient either dry on the tongue, or in solution, or admixed with a small quantity of water, physicians frequently direct them to be enclosed in capsules or wafers, with the view to disguise the taste. The filling of definite quantities of a powder into capsules is rather troublesome, on account of the small orifice of the latter; and to facilitate the operation recourse is had to a device especially designed for that purpose. Small blocks of hard wood are provided with 12 or 24 sockets of such depth that the capsules, when placed therein, shall project about one-third above the edge; another piece of wood, with perforations corresponding to the sockets, is placed over the lower block, after the capsules have been inserted, and then, by means of a suitable funnel (of hard rubber or metal), the powder is transferred to the capsules and somewhat compressed with a plunger exactly fitting the throat of the funnel and the capsule. After all the capsules have been filled the upper perforated block is removed and the cover slipped over the projecting ends of each capsule. For the various sizes of capsules different blocks and funnels are required. In Figs. 287 and 288 are shown the blocks and a suitable funnel; the latter has a wide rim flattened on one side and a short tube, whereby the powder is more conveniently fed into the capsules.

To facilitate the filling of simple and compound powders into gelatin capsules, an apparatus known as Ihrig's capsule-filler was devised in 1899, for which it is claimed that the filling can be done more expeditiously than by any other method and with remarkable

accuracy as to weight. As shown in Fig. 289, the apparatus consists of a stationary metal base with a square polished movable plate or table having perforations for holding the various sizes of capsules, and which can be raised or lowered by means of a thumb-screw. The perforations are arranged in fields of 60 for each Nos. 2, 3, 4, 5, and

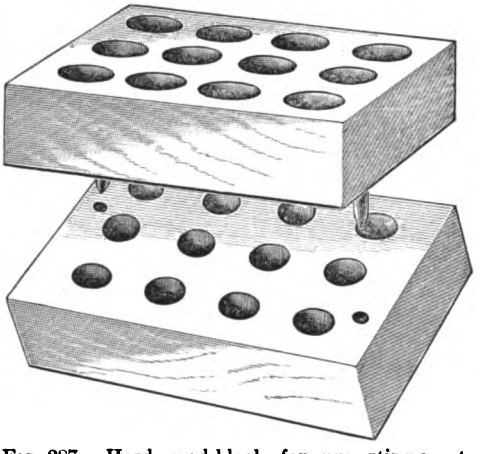


FIG. 287.—Hard wood blocks for supporting empty capsules while being filled.

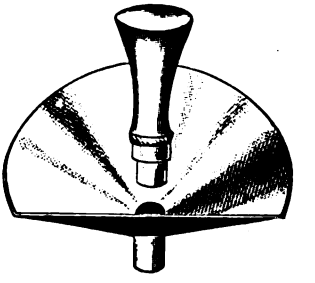


FIG. 288.—Davenport's funnel and plunger for filling capsules.

00 gelatin capsules, and of 56 for each Nos. 1 and 0. When in position for filling, the lower portion of the capsules should rest on the base and the upper plate be raised so that the top of the capsules is slightly below the surface of the upper plate. A metal square accompanying each apparatus is next placed in proper position, as shown in the illustration, so as to separate the capsules to be filled from perforations

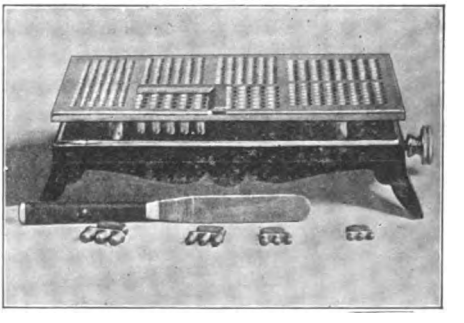


FIG. 289.

not in use, and the powder having been distributed with a spatula or camel-hair pencil, is pressed into the capsules by means of a metallic triple punch, as shown in Fig. 290. In order to enable the operator to put the tops on the capsules, the upper plate is lowered, as shown in Fig. 291, when the cap can be quickly adjusted. An important

point in filling powders into gelatin capsules is to use capsules of the proper size to hold the required quantity of powder nicely, and this

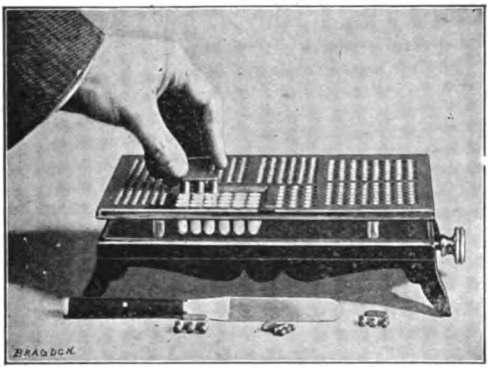


FIG. 290.

must be determined tentatively. Manufacturers of gelatin capsules suggest the following guide for approximate capacity of empty capsules, which will enable pharmacists to make a suitable selection without

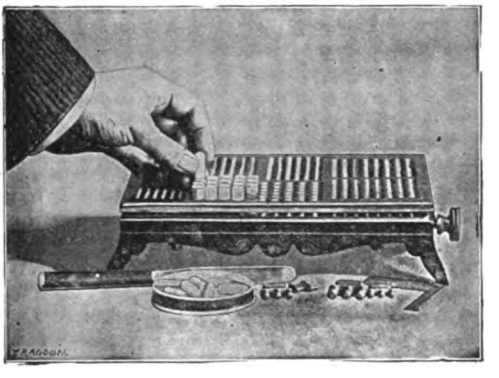


FIG. 291.

much trouble, bearing in mind, however, that the capacity varies according to the degree of compression exerted in filling:

Size of Capsule.	No.	00.	0.	1.	2.	3.	4.	5.
Bismuth Subnitrate	Grs.	20	14	10	8	6	4	2
Cinchonidine Sulphate	Grs.	8	6	4	3	2	1½	¾
Dover's Powder	Grs.	12	8	6	4	3	2	1
Powdered Aloes	Grs.	10	7	5	4	3	2	1
Powdered Rhubarb	Grs.	12	8	6	4	3	2	1
Quinine Sulphate	Grs.	8	6	4	3	2	1½	¾
Salicin	Grs.	10	7	5	4	3	2	1
Salicylic Acid	Grs.	8	6	4	3	2	1½	¾

Another simple apparatus for filling powders uniformly into gelatin capsules, and well adapted for use at the dispensing counter, is shown in Figs. 292 and 293.[1] It consists of three metal plates, each having four rows of perforations, suitably hinged together and fastened to a metal base resting on a wooden block, and is so constructed that 24 capsules of either of the four sizes, Nos. 0, 1, 2, or 3, can be filled at one time.

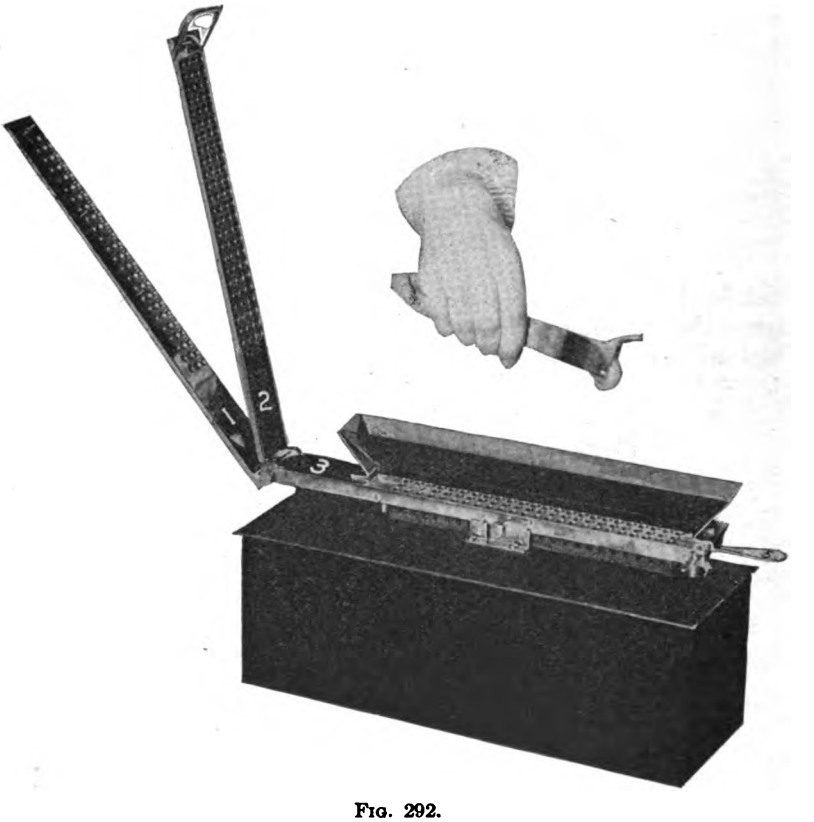


FIG. 292.

When capsules are to be filled, plate 1 is raised, the sliding catch on the front of the apparatus being moved to the right as far as possible, so as to keep the plate rigid, and the particular size of capsules required is placed in plate 2, as shown in Fig. 293, with the tops of the capsules upward. Plate 1 is then lowered and fastened to plate 2 by means of the handle attached to the latter, as shown in Fig. 294.

The two plates are now raised while holding the lever 5 with the right hand, whereby the tops of the capsules are removed, and then moving

[1] This capsule filler can be obtained from Sharp & Dohme, Baltimore, Md.; also larger sizes of the same, filling 100 to 300 capsules at a time.

the lever back to its original position, causes the capsules in plate 3 to drop and rest on the base of the apparatus.

FIG. 293.

FIG. 294.

The filling box is then placed in position on plate 3, as shown in Fig. 292, by inserting the square-shouldered pin on the bottom of the

box in the slot on the left of the plate and the round pin in the hole on the right of the plate, and held firmly by means of a small lever. The powder having been put into the filling box, is pushed into the holes and down into the capsules with the square rubber tip attached to the roller shown in Fig. 292; if all the powder cannot be pushed into the capsules, the balance is rolled in by means of the roller and the contents of the holes are pushed out with pegs corresponding to the holes in the filling box.

The filling box is now removed, the sliding catch on the front of the apparatus released by moving it as far to the left as possible, and plates 1 and 2 lowered together, when by a sharp downward pressure with both hands on plate 1, as shown in Fig. 295, the tops of the capsules

FIG. 295.

are replaced. If plates 1 and 2 are then raised together, the capsules can be easily removed by gently tapping the exposed ends with a rubber-tipped mallet.

Two filling boxes are supplied with the apparatus, one for No. 0 and No. 1 capsules and the other for No. 2 and No. 3 capsules.

The use of wafers is not so much in vogue in this country as in Europe, but they are, in many respects, preferable to capsules; less compression of the material is necessary, and the envelope, made of rice flour, is more readily disintegrated in the stomach. Sometimes small square or circular sheets of wafer paper are ordered, and the patient is directed to enclose each dose as wanted; this is done by dipping the wafer into cold water, whereby it is rendered flaccid; it

is then laid over a spoon, the powder placed in the center, and, the edges having been folded over, it is swallowed with a draught of water.

The small round wafers known as cachets are intended to be filled and sealed by pharmacists. Various appliances have been proposed, of which that extensively used in Europe in connection with Mohr-

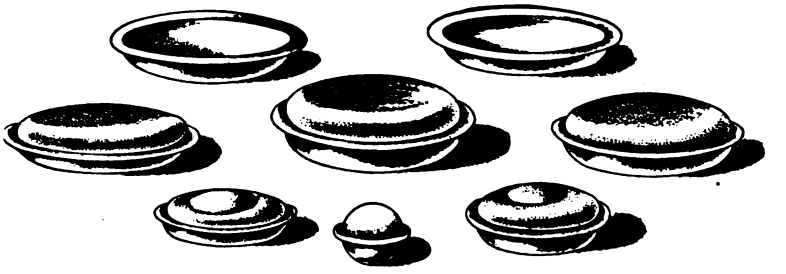


FIG. 296.—"Konseals" or rice flour cachets.

stadt's cachets is decidedly the most desirable, as it is simple in construction and quickly operated; the device is sold in this country by J. M. Grosvenor & Co., of Boston, as the "Konseal" filling and closing apparatus, and is fully illustrated and described further on. The use of the word "konseal" in place of cachets or wafers does not strike

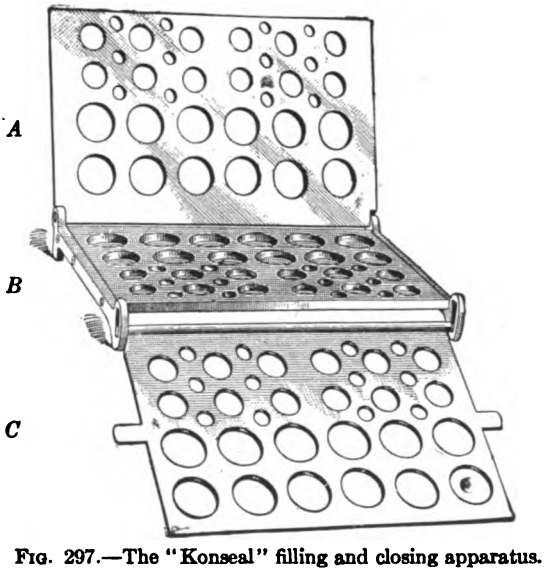


FIG. 297.—The "Konseal" filling and closing apparatus.

one as particularly appropriate, and is to be regretted. The "konseals," or cachets, are concave disks made of rice flour and water; they are of convenient form, perfectly digestible, keep permanently for years, and are prepared in six sizes, shown in Fig. 296, varying in capacity from 1 to 10 or 20 grains of dry powder.

The "Konseal" filling and closing apparatus consists of three nickelled plates suitably hinged (see Fig. 297); the center plate *B* is provided with 36 concave depressions, to suit the different sizes of wafers, and the two other plates (*A* and *C*) are perforated in a manner to correspond exactly to the depressions in *B*. The wafers are first

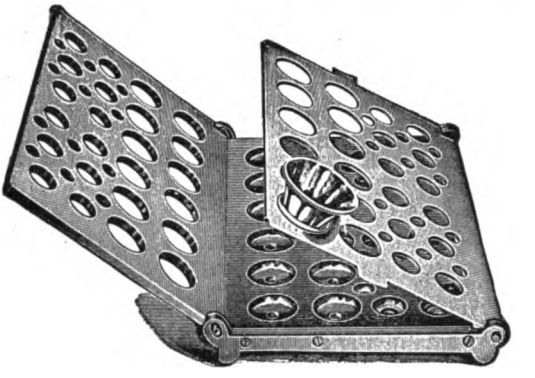


FIG. 298.

pressed into the spaces of *A* and *B* adapted for the particular size selected; one of the short funnels accompanying the apparatus having been inserted into the proper perforation of plate *C*, the latter is folded over on to plate *B*, as shown in Fig. 298. The powders are next poured into the wafers, as shown in Fig. 299, and, if necessary, owing to large bulk, are slightly compressed with the thimble furnished for the purpose; small quantities of the powder can be conveniently

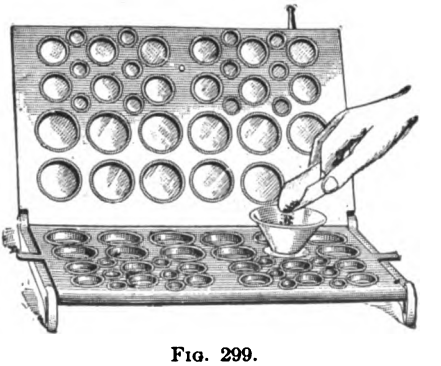


FIG. 299.

fed into the wafers without the use of funnel or thimble. When the required number of wafers has been filled plate *C* is turned back from plate *B*, and the dampening roller (not too wet) passed over the wafers in plate *A*, as shown in Fig. 300, whereby the edges of the wafers are sufficiently moistened to cause them to adhere closely to the other

wafers when plate *A* is closed down over plate *B* with a little pressure. Finally, on opening the apparatus, the sealed wafers will be found adhering to plate *A*, and can be easily pushed out by the fingers or with the thimbles.

When powders are to be dispensed in wafers it will, of course, be necessary first to make the required number of divisions on paper,

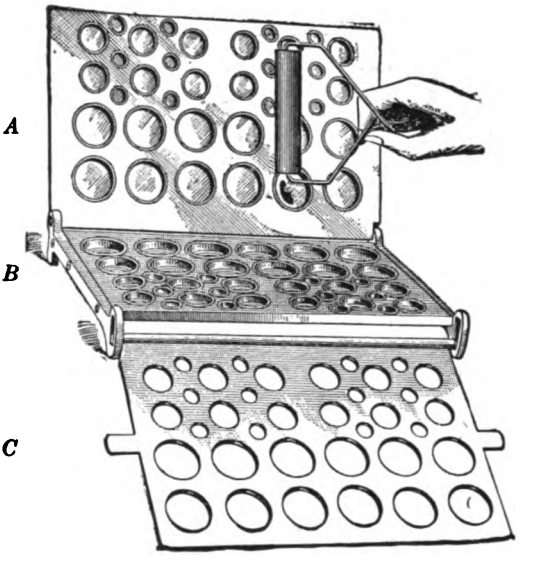


FIG. 300.

either by weighing or measuring with the eye; in Europe a graduated glass tube with hard rubber piston is said to be used for the same purpose.

The Pharmacopœia furnishes formulas for the preparation of 7 compound powders, but directs the division into doses in only 1 case. The following is a list of the official powders and their composition:

COMPOUND POWDERS OF THE U. S. PHARMACOPŒIA.

Latin name.	English name.	Composition.		
Pulvis Aromaticus	Aromatic Powder	Saigon Cinnamon	35.0	Gms.
		Ginger	35.0	"
		Cardamom seed (deprived of pericarp)	15.0	"
		Nutmeg	15.0	"
Pulvis Cretæ Compositus	Compound Chalk Powder	Prepared Chalk	30.0	"
		Acacia	20.0	"
		Sugar	50.0	"
Pulvis Effervescens Compositus	Compound Effervescing Powder (Seidlitz Powder)	Sodium Bicarbonate	2.5	"
		Potassium and Sodium Tartrate	7.5	"
		Tartaric Acid	2.166 +	"

Latin name.	English name.	Composition.		
Pulvis Glycyrrhizæ Compositus	Compound Powder of Licorice	Senna	180.0	Gms.
		Glycyrrhiza	236.0	"
		Washed Sulphur	80.0	"
		Oil of Fennel	4.0	"
		Sugar	500.0	"
Pulvis Ipecacuanhæ et Opii	Powder of Ipecac and Opium (Dover's Powder)	Ipecac	10.0	"
		Opium	10.0	"
		Sugar of Milk	80.0	"
Pulvis Jalapæ Compositus (Pulvis Purgans)	Compound Powder of Jalap	Jalap	35.0	"
		Potassium Bitartrate	65.0	"
Pulvis Rhei Compositus	Compound Powder of Rhubarb	Rhubarb	25.0	"
		Magnesia	65.0	"
		Ginger	10.0	"

The *National Formulary* recommends the preparation of 14 mixed powders, as shown below:

Latin name.	English name.	Composition.
Pulvis Acetanilidi Compositus	Compound Acetanilid Powder	Contains acetanilid, caffein and sodium bicarbonate.
Pulvis Aloes et Canellæ	Powder of Aloes and Canella	Contains aloes and canella. It is popularly called Hiera Picra.
Pulvis Antimonialis	Antimonial Powder (James' Powder)	Contains antimony oxide and precipitated calcium phosphate.
Pulvis Antisepticus	Soluble Antiseptic Powder	Contains salicylic acid, phenol (carbolic acid), eucalyptol, menthol, thymol, zinc sulphate, and boric acid. It is also known as Pulvis Antisepticus Solubilis.
Pulvis Aromaticus Rubefaciens	Rubefacient Spice Powder	Contains saigon cinnamon, cloves, ginger, and capsicum.
Pulvis Cretæ Aromaticus	Aromatic Chalk Powder	Contains cinnamon, nutmeg, cloves, cardamom, prepared chalk, and sugar.
Pulvis Cretæ Aromaticus cum Opii	Aromatic Chalk Powder with Opium	Contains besides the ingredients of the previous powder 2½ per cent. of opium.
Pulvis Gambir Compositus (Pulvis Catechu Compositus)	Compound Powder of Gambir	Contains gambir, kino, krameria, Saigon cinnamon, and nutmeg.
Pulvis Hydrargyri Chloridi Mitis et Jalapæ	Powder of Mild Chloride of Mercury and Jalap	Contains mild chloride of mercury and jalap. This powder is sometimes called for by the simple name Calomel and Jalap.
Pulvis Kino et Opii Compositus	Compound Powder of Kino and Opium	Contains kino, cinnamon, and 5 per cent. of opium.
Pulvis Myricæ Compositus	Compound Powder of Bayberry	Contains bark of bayberry root, ginger, capsicum, and cloves. This powder is popularly known as Composition.
Pulvis Pancreaticus Compositus	Compound Pancreatic Powder)	Contains pancreatin and sodium bicarbonate. It is also known as Peptonizing Powder.
Pulvis Rhei et Magnesiæ Anisatus	Anisated Powder of Rhubarb and Magnesia (Compound Anise Powder)	Contains rhubarb, heavy calcined magnesia, and anethol; the anethol is mixed with a small quantity of alcohol, which is subsequently dissipated during the trituration.
Pulvis Talci Compositus	Compound Powder of Talc (Boro- Salicylated Powder of Talc)	Contains salicylic acid, boric acid, and talc.

SPECIAL REMARKS.

In the case of compound chalk powder and compound jalap powder, the ingredients being already in a state of fine powder, simple admixture with light trituration is necessary.

Pulvis Acetanilidi Compositus (*Compound Acetanilid Powder*).—This preparation, which has been transferred from the Pharmacopœia to the *National Formulary*, contains 70 per cent. of acetanilid, 10 per cent. of caffeine, and 20 per cent. of sodium bicarbonate.

Pulvis Aromaticus (*Aromatic Powder*).—Cardamom seed deprived of the pericarp is directed, because the latter is inert and cannot be reduced to fine powder; the crushed seed and freshly grated nutmeg can readily be brought to a state of fine powder by trituration with about one-half of the cinnamon, using at the same time slight pressure.

Pulvis Effervescens Compositus (*Seidlitz Powder*).—The so-called "Seidlitz Mixture" of commerce is not always of the composition prescribed by the Pharmacopœia; hence it is better to make it, as wanted, by mixing 1 part of sodium bicarbonate with 3 parts of Rochelle Salt. The alkaline mixture is usually put up in blue papers and the acid powder in white paper. The small wooden measures intended for rapid division of the powders are, as a rule, not uniform; moreover, the quantity of material that can be compressed into these measures varies considerably with the condition of the atmosphere which renders them unreliable; hence the prescribed quantities should be weighed for each paper, being 10 Gms. (155 grains) of Seidlitz Mixture and 2.166+ Gms. (33.5 grains) of tartaric acid. The powders should be protected against dampness, and it will be found advantageous to dispense the tartaric acid in parchment paper.

The Pharmacopœia requires that the weight of the alkaline mixture in the blue paper shall not be less than 9.5 Gms., nor more than 10.5 Gms., and that upon assay of the mixture, it shall be shown to contain not less than 23 per cent., nor more than 27 per cent., of sodium bicarbonate and not less than 73 per cent., nor more than 78 per cent., of potassium and sodium tartrate.

Pulvis Glycyrrhizæ Compositus (*Compound Licorice Powder*).—By triturating the oil of fennel with a part of the sugar, before adding the other ingredients, its distribution in the powder is greatly facilitated. The use of oil in place of powdered fennel is advantageous, as the finished mixture can then readily be passed through a No. 80 sieve, and the finer the powder, the better it is; moreover, the product will not assume by age that disagreeable odor which has been observed when the powdered seed is used.

Pulvis Ipecacuanhæ et Opii (*Powder of Ipecac and Opium, or Dover's Powder*).—The Pharmacopœia directs sugar of milk to be used in rather coarse powder, so that the fragments of crystals, being very hard, may serve to grind the vegetable powders to an impalpable condition during the necessary prolonged trituration. Since the

finished product contains 10 per cent. each of ipecac and opium, an average adult dose, 0.648 Gm. (10 grains), of the powder will represent 0.0648 Gm. (1 grain) of each active ingredient. Dover's powder is a favorite diaphoretic.

Pulvis Rhei Compositus (*Compound Rhubarb Powder*).—The best plan for thoroughly blending the magnesia with the rhubarb and ginger will be to mix the last-named two powders first, then add the magnesia, in small quantities at a time, triturating without pressure, and, finally, pass the whole mixture through a bolting-cloth sieve.

TRITURATIONS.

Under this head the Pharmacopœia recognizes mixtures of remedial agents and sugar of milk, in the form of a very fine powder, made in such proportions that each Gm. of the mixture shall contain 0.100 Gm. of the active ingredient, or 1 grain represents $\frac{1}{10}$ of a grain. The general official directions for making triturations are to mix the substance in a mortar with an equal weight of sugar of milk, both in moderately fine powder, and then to triturate thoroughly together, adding fresh portions of sugar of milk from time to time, until 9 parts of the latter shall have been mixed with 1 part of the substance, and the whole reduced to a very fine powder. The advantage of using moderately fine powder in the beginning consists in the more intimate admixture of the ingredients brought about by the prolonged trituration necessary for reduction to fine powder.

But one trituration is officially designated, namely, "Trituration of Elaterin"; this is a mixture of 10 Gms. of elaterin and 90 Gms. of sugar of milk, made according to the general directions given above.

OIL SUGARS.

Powders of this class are chiefly used as correctives or flavoring agents, and are prescribed by physicians under the name Oleosacchara or Elæosacchara. These are extensively employed in Europe, particularly in Germany, and are recognized in the *National Formulary*, but not in our Pharmacopœia.

Oil sugars are composed of powdered cane sugar and volatile oil only, each drachm of the former requiring the addition of 2 drops of the latter, the two being thoroughly mixed by trituration; they should be freshly made when wanted. When prescribed, the particular kind is designated by specifying the name of the oil to be used; thus, oleosaccharum or elæosaccharum anisi, menthæ piperitæ, fœniculi limonis, etc., meaning oil sugar of anise, peppermint, fennel, lemon, etc.

CHAPTER XXXII.

GRANULAR EFFERVESCENT SALTS.

THE administration of remedial agents in the form of effervescent draughts has become quite popular during the past thirty years, and, as the solutions are only agreeable when freshly made, it is necessary to have the remedies in convenient form for extemporaneous preparation of the draught. Such a form is presented by the granular effervescent salts of the market. While the Pharmacopœia recognizes but 3 preparations of this class, and the *National Formulary* 7, a very large number is offered by manufacturers, and, as they are easily made, without elaborate apparatus and appliances, their preparation is within the reach of all pharmacists. The combination consists of the active medicinal ingredients, the effervescent agents, and sometimes sugar, to improve the taste. As a base for producing the effervescent draught, sodium bicarbonate, with citric or tartaric acid, or a mixture of the two acids is employed. Effervescent granules made with citric acid are preferable to those made with tartaric acid, and will keep better, since they are much firmer; as a rule, a mixture of the two acids is used.

All the required ingredients for effervescent granules must be used in fine powders, preferably No. 60, and thoroughly mixed before an attempt at granulating is made; trituration in a mortar is not desirable, since the resulting pressure is likely to cause reaction between the sodium bicarbonate and acid, hence intimate admixture is best effected by passing the mingled powders several times through a coarser sieve, preferably No. 30. The addition of sugar should be avoided whenever possible, on account of its tendency to discolor the granules, but if used it will be found advantageous to mix it thoroughly with the sodium bicarbonate before adding the acids. The method of granulating will vary with different operators; for small quantities of material, dampening of the mixed powders with alcohol and then rubbing the paste through a sieve offers a very convenient plan, while for larger operations the fusion method will develop the necessary adhesiveness. Strong alcohol only should be used, not below 94 per cent., for making a stiff doughy paste that can be just rubbed through a sieve, as otherwise the presence of much water will cause more reaction between the alkali and acids and yield a soft mass, which will not remain in separate granules while drying. The quantity of alcohol necessary will naturally vary with the composition of the mixture; whenever citric acid or salts containing water of crystallization are present, a smaller quantity must be used. The granules

having been obtained are finally dried thoroughly, preferably in drying closets kept at a constant temperature, and not heated above 50° or 54° C. (122° or 129° F.) to avoid decomposition of the sodium bicarbonate. A No. 6 or No. 8 sieve yields the most desirable size of granules, from which the fine particles, which are invariably formed along with the coarser, can be readily separated by shaking in another suitable sieve.

All effervescent salts should be preserved in well stoppered bottles, in a dry place, as they are inclined to attract moisture from the air and thus rapidly deteriorate.

The pharmacopœial directions for the preparation of granular effervescent salts are to place the mixed powders on a plate of glass or in a suitable dish, in an oven heated to between 93° and 104° C. (199.4° and 219.2° F.). When the mixture, by the aid of careful manipulation with a wooden spatula, has acquired a moist consistence, it is to be rubbed through a No. 6 tinned iron sieve, the resulting granules being dried at a temperature not exceeding 54° C. (129.2° F.).

The formulas of the Pharmacopœia for making granular effervescent salts are defective, as experience has shown, in that the amount of citric acid ordered is too low to yield good granules, and no allowance is made for loss of weight by escape of moisture and carbon dioxide during the process of manufacture, which influences the percentage content of medicinal ingredient in the finished product; this loss varies and sometimes reaches 15 per cent. Moreover the powdered citric acid should be added last to the mixture of the other ingredients, for if there be much humidity in the air, the mixture will lump and cake, and when fused, will be full of wet spots, a very undesirable condition. The amount of citric acid to be used in a formula is an important factor and will depend upon the particular method of manufacture to be followed, varying from 16 to 25 per cent. of the calculated yield of finished product.

The *National Formulary* gives directions for making granular effervescent salts by two different methods; they are practically identical with the following suggestions of Lowry and Barnett, which have been found to yield satisfactory results.

The sodium bicarbonate, medicinal ingredient, and tartaric acid, all in No. 60 powder, should be passed successively through a No. 30 sieve; the citric acid, powdered from uneffloresced crystals just before using so as to avoid loss of moisture, is then passed through the sieve and the whole mixed without pressure. If small quantities of the salt are to be made, say from 100 to 250 Gms., the mixed powders are transferred to the inner boiler of an agateware rice boiler, in the outer boiler of which water is boiling briskly, and then stirred constantly until thoroughly dry; this operation requires about eight or ten minutes. The salt is finally passed through a suitable sieve to separate the granules from any powder formed. This method is admirably adapted for the needs of the retail pharmacist, but does not yield as large nor as perfect granules as the

method followed by large manufacturers, who use an increased amount of citric acid and proceed as follows:

The powders previously mixed in the manner stated above are spread evenly about three-eighths of an inch thick, on a sheet of paper resting on a canvas tray, a glass plate, or a shallow enameled-ware dish. Then place in an oven heated to not less than 95° C. (204° F.) and not over 105° C. (221° F.), and allow to remain there without stirring until fusion has taken place and the mixture has assumed the consistency of stiff bread dough, but not quite pasty. This is the critical part of the whole operation and requires some practical experience. The mass is immediately transferred to a No. 5 or No. 6 tinned iron sieve and forced through, a pestle being sometimes necessary for the few hard granules that may have formed. The granules are then spread out on a tray and dried in an oven at a temperature not exceeding 50° C. (122° F.). The time necessary for complete drying depends on atmospheric conditions and may vary from three to six hours; when a vacuum dryer is used, as is generally the case in large manufacturing establishments, the time is very materially reduced.

The quantities of citric and tartaric acids and sodium bicarbonate in a formula must be carefully calculated, and will vary with the weight of finished product desired and the proportion of medicinal ingredient used. Allowance must also be made for loss of weight, due to escape of moisture and carbon dioxide, which varies from 10 to 15 per cent. Large quantities of granular effervescent salts require relatively more citric acid than small quantities, owing to the different modes of manipulation explained above, as shown in the following two formulas:

To make 250 Gms. of granular effervescent sodium phosphate use citric acid, 41.25 Gms.; anhydrous sodium phosphate, 50 Gms.; tartaric acid, 72.6 Gms.; sodium bicarbonate, 132 Gms.; of which the citric acid requires about 50 Gms. and the tartaric acid about 82 Gms. (Loss about 15 per cent.)

To make 5000 Gms. of granular effervescent sodium phosphate use citric acid, 1250 Gms.; anhydrous sodium phosphate, 1000 Gms.; tartaric acid, 901 Gms.; sodium bicarbonate, 2516 Gms., of which the citric acid requires about 1500 Gms. and the tartaric acid about 1016 Gms. (Loss about 12 per cent.)

In constructing a formula for granular effervescent salts the first thing necessary is to calculate the quantities of acid and alkali required for the effervescent base, which latter should never be less than one-half of the weight of the intended finished product. Experience has taught that in order to obtain 100 parts of finished granules, 120 parts of effervescent base will be required for the double-boiler method of granulation explained above, whereas but 115 parts are necessary for the oven method used for larger quantities, the loss in both cases, as already stated, being due to escape of moisture and carbon dioxide.

For the double-boiler method 16.5 parts of citric acid should be

used for every 120 parts of effervescent base, which require 19.8 (acutally 19.79) parts of sodium bicarbonate for neutralization; this would leave 120−36.3=83.7 parts to be provided for by addition of tartaric acid and sodium bicarbonate. These 83.7 parts must consist of 47.5 per cent., or 39.76 parts of tartaric acid, and 52.5 per cent., or 43.94 parts of sodium bicarbonate, since 100 parts of the acid require 112 (actually 111.97+) parts of sodium bicarbonate for neutralization.

In the case of the oven method 25 parts of citric acid should be used for every 115 parts of effervescent base needed, which require 30 parts of sodium bicarbonate for neutralization; this leaves 115−55=60 parts to be provided for by addition of tartaric acid and sodium bicarbonate. These 60 parts must consist of 47.5 per cent., or 28.5 parts of tartaric acid and 52.5 per cent., or 31.5 parts of sodium bicarbonate.

GRANULAR EFFERVESCENT SALTS OF THE U. S. PHARMACOPŒIA.

Latin name.	English name.	Composition.	
Caffeina Citrata Effervescens	Effervescent Citrated Caffeine	Citrated Caffeine	40 Gms.
		Sodium Bicarbonate	570 "
		Tartaric Acid	300 "
		Citric Acid	195 "
Potassii Citras Effervescens	Effervescent Potassium Citrate	Potassium Citrate	200 "
		Sodium Bicarbonate	477 "
		Tartaric Acid	252 "
		Citric Acid	162 "
Sodii Phosphas Effervescens	Effervescent Sodium Phosphate	Exsiccated Sodium Phosphate	200 "
		Sodium Bicarbonate	477 "
		Tartaric Acid	252 "
		Citric Acid	162 "

GRANULAR EFFERVESCENT SALTS OF THE NATIONAL FORMULARY.

Latin name.	English name.	Composition.
Sal Carolinum Factitium Effervescens	Effervescent Artificial Carlsbad Salt	Artificial Carlsbad salt, sodium bicarbonate, citric acid, and tartaric acid.
Sal Kissingense Factitium Effervescens	Effervescent Artificial Kissingen Salt	Artificial Kissingen salt, sodium bicarbonate, citric acid, and tartaric acid.
Sal Lithii Citratis Effervescens	Effervescent Salt of Lithium Citrate	Lithium citrate, sodium bicarbonate, citric acid, and tartaric acid.
Sal Potassii Bromidi Effervescens	Effervescent Salt of Potassium Bromide	Potassium bromide, sodium bicarbonate, citric acid, and tartaric acid.
Sal Potassii Bromidi Effervescens Compositum	Compound Effervescent Salt of Potassium Bromide (Effervescent Potassium Bromide with Caffeine)	Potassium bromide, caffeine, lithium carbonate, sodium bicarbonate, citric acid, and tartaric acid.
Sal Vichyanum Factitium Effervescens	Effervescent Artificial Vichy Salt	Artificial Vichy salt, sodium bicarbonate, citric acid, and tartaric acid.
Sal Vichyanum Factitium Effervescens cum Lithio	Effervescent Artificial Vichy Salt with Lithium	Artificial Vichy salt, lithium citrate, sodium bicarbonate, citric acid, and tartaric acid.

CHAPTER XXXIII.

OINTMENTS, CERATES, AND ALLIED PREPARATIONS.

Both classes of these preparations are intended solely for external application; they are of similar composition, of unctuous character, differing, however, from each other in degree of firmness and fusibility. While the U. S. Pharmacopœia officially recognizes the difference between ointments and cerates, this distinction is not maintained, as a rule, in Europe. The British and German Pharmacopœias designate both classes as ointments; in France the term *pommade* is applied to all ointments made with a purely fatty base, even if a small proportion of wax be present; while the term *onguent* is only used if a resinous or similar substance has been added, the name *cérat* being reserved for mixtures of fat and wax containing at least as much wax as our own cerates.

In the preparation of ointments and cerates it is of importance that perfectly smooth, homogeneous mixtures be obtained, and that the fatty vehicle be absolutely free from rancidity, since they are often applied to tender excoriated surfaces, and would otherwise prove a source of irritation instead of a soothing application. Lumps or gritty particles in ointments indicate unpardonable carelessness on the part of the dispenser.

Ointments and cerates made with yellow wax or rosin are less liable to deterioration than when made with white wax, since the latter during the bleaching process undergoes incipient rancidity; they should be preserved in well glazed, covered porcelain jars, and kept in a dry, moderately cool place. The true porcelain jars, although somewhat expensive, are to be preferred, as they are strictly impermeable to grease and can be thoroughly cleaned with hot water and lye whenever empty; the author had a set of these jars in constant use for over fifteen years without ever having an ointment turn rancid in them. Glass stock jars are offered at a much lower price, but will often crack while being cleaned, particularly with hot water, yet they are vastly superior to the ordinary white china or queensware covered jar, since the glazing of the latter soon becomes full of fine cracks, through which the fat permeates and, gradually turning rancid, contaminates the contents of the jar; moreover, no amount of washing will remove the rancid grease entirely from the pores of the jars, hence they soon become unfit for use. The sweet condition of ointments and cerates cannot be preserved without proper care and cleanliness; unfortunately these precautions are not always observed by pharmacists.

OINTMENTS.

Ointments may be conveniently divided into distinct classes in regard to their therapeutic effect, thus: 1. Protective ointments, which are non-absorbable in character and act strictly epidermatically —that is, on the outer skin or cuticle. 2. Emollient ointments, which have nutritive or absorbefacient properties and act endermatically or by penetrating into the skin. 3. Ointments which produce systemic or constitutional effects, and must therefore be absorbable, acting diadermatically by penetrating not only into but through the skin. This difference in the therapeutic effects desired necessitates careful selection of the vehicle intended for exhibition of the medicinal agents.

Ointment Bases or Vehicles.—Non-absorbable ointments intended to produce some medicinal effect on the outer skin, such as astringent, counter-irritant, antiseptic, germicidal or similar effect, or possibly to act as protective agents, may therefore be made with petrolatum or a mixture of the same with hard paraffin, which latter combination is to be preferred in warm weather on account of its higher fusing-point. The British and German Pharmacopœias recognize such a vehicle under the name *unguentum paraffini*, which in the former case consists of hard paraffin 3 parts and soft paraffin 4 parts, and in the latter case of hard paraffin 1 part and liquid paraffin 7 parts; hence the British preparation is much the firmer of the two. For emollient ointments designed to penetrate into the skin for the purpose of producing a deeper local effect, such as anodyne, stimulant, resolvent, etc., preference should be given to lard, lard mixed with wax, lard and oil, oil and wax, or oil, wax, and spermaceti. As stated on page 220, the lard to be used for ointments should be free from water and other impurities. The absorbent properties of these bodies permit the admixture of medicinal agents in the form of solution either in water, alcohol, glycerin, oleic acid, or oil. In the last group of ointments, which are intended to produce systemic or constitutional effects, vehicles should be employed which penetrate not only into but through the skin, thereby permitting the absorption of the remedial agent present. No substance is known to possess these properties to a greater degree than wool fat and the modified form of the same, officially recognized under the name hydrous wool fat, and commonly designated as lanolin, which are themselves closely related to the fat secreted in the sebaceous glands of the human body. Wool fat can readily be combined with its own weight of water and even larger quantities, whereas lard takes up only about one-fifth of its weight of water and soft paraffins not more than 10 per cent.

The official glycerite of starch is sometimes used by physicians under the name of *plasma* or *plasma glycerini* as a vehicle for ointments, in place of lard or petrolatum. It possesses the advantage of not being of a fatty nature, and hence easily removed by washing

with water, and never becoming rancid; but as it is somewhat hygroscopic it must be preserved in well closed jars. It is especially preferred by oculists for the application of lead acetate, mercuric oxide, and similar substances to the eyelids.

Dermatologists have long been looking for an ointment base or vehicle which, while non-irritating, should not be of a greasy nature if possible, so as to render its use more convenient and agreeable to patients. Numerous substances have been suggested, such as solvine or polysolve and oleite, which are alkali sulpho-ricinoleates, and as such miscible with water; gelatole, a mixture of oleite and gelatin, and similar semisolid preparations, to be applied in the form of a thin layer or varnish-like coating. The most successful in this respect appears to have been a vehicle composed of casein, glycerin, and soft paraffin, which is used in Europe under the name *unguentum caseini*. According to Dr. Unna, the originator of this preparation, it is made by separating casein from milk, entirely deprived of its fat or cream, by addition of rennet at a temperature of about 35° C. (95° F.), collecting the curd, washing free from acid, and finally drying. Of the dried and powdered casein, 1400 parts are dissolved in 5000 parts of a weak alkaline solution, containing 34.5 parts of potassium hydroxide and 8.5 parts of sodium hydroxide. To this solution add 50 parts of carbolic acid and 700 parts of glycerin, and, when dissolved, 50 parts of zinc oxide and 2100 parts of vaselin are incorporated, and finally sufficient water is added to bring the total weight up to 10,000 parts. The finished preparation resembles very soft cold cream or thick condensed milk, is free from greasiness, and is said to be readily removed from the skin with water. Casein ointment is incompatible with acids and acid salts, but can be mixed with metallic mercury, tar, balsam of Peru, etc.; powdered vegetable or mineral substances should first be mixed with a little vaselin before incorporation.

Preparation of Ointments.—As regards the mode of preparation of ointments, three distinct methods are followed, namely, by fusion, by incorporation of the medicinal agent with a suitable vehicle, and by chemical action. When ointments are to be made by fusion, those constituents having the highest fusing point, as rosin, wax, and spermaceti, should be heated first, and, when nearly melted, the lard or oil added, bearing in mind that as long as some of the particles remain unmelted there is no danger from the continued application of heat, which should, however, be withdrawn in time to avoid a rise in temperature of the melted fats (see page 98). Fusion of ointments is preferably performed on a waterbath, in round-bottom pans or evaporating dishes, and, if dirt be present, the melted mixture may be decanted, or, if necessary, strained through cheesecloth into a previously warmed dish or mortar; the liquid should then be stirred until a homogeneous soft mass results, after which it may be set aside and allowed to stiffen by further gradual cooling. The stirring of melted fats while cooling is essential to insure a perfectly smooth

product, since fats are composed of solid and liquid bodies, which, during the cooling process, become partially separated, producing a granular solid on congealing, if allowed to cool at perfect rest, as may be seen in the case of plain lard; moreover, in a mixture of melted fats those having a higher fusing point would naturally congeal earlier than the rest; therefore, unless an intimate mixture be kept up by constant stirring, separation would ensue and a lumpy ointment result. The point of danger may be said to have been passed when the melted ointment, being continually stirred, has so far cooled that a uniform thick, creamy mass is obtained; for stirring, a broad wooden spatula will be found advantageous. When large quantities of aqueous liquids are to be incorporated with melted fats, as in the case of rose water ointment, the liquid should be warmed and then slowly added, with constant trituration, to the mixed fats previously somewhat cooled; otherwise the less fusible constituents will be chilled by the cold liquid and separate in granular form, thus preventing a smooth ointment. The Pharmacopœia directs the following ointments to be made by fusion:

Latin name.	English name.	Composition.	
Unguentum	Ointment	Benzoinated Lard	800 Gms.
		White Wax	200 "
Unguentum Aquæ Rosæ	Ointment of Rose Water (Cold Cream)	Spermaceti	125 "
		White Wax	120 "
		Expressed Oil of Almond	560 "
		Stronger Rose Water	190 "
		Sodium Borate	5 "
Unguentum Diachylon	Diachylon Ointment	Lead Plaster	500 "
		White Paraffin	490 "
		Oil of Lavender	10 "
Unguentum Picis Liquidæ	Tar Ointment	Tar	500 "
		Lard	350 "
		Yellow Wax	150 "

In the preparation of the official rose water ointment it is essential that a perfect solution of the borax in the rose water be effected, and to prevent sudden chilling of the fatty mixture the borax solution should be warmed somewhat. Constant stirring is necessary to produce a smooth, creamy ointment. The addition of borax to the official rose water ointment gives the latter a whiter and more creamy appearance, but at the same times interferes with the admixture of certain chemicals, such as calomel, yellow mercuric oxide, etc., causing discoloration of the ointment. Vegetable or mineral powders cannot be mixed in quantity with rose water ointment without forcing the water out of combination.

Unless the lead plaster for diachylon ointment be fresh, it is best to remove the darkened dry exterior, thus obtaining a lighter colored and softer ointment; the white paraffin must be added when the plaster is nearly melted on a water-bath, and a better mixture will result if the heat be continued for five or ten minutes afterward, so as to blend the paraffin and plaster more thoroughly. The melted

mixture must be stirred until creamy, when the oil of lavender may be added, the whole transferred to a jar and allowed to cool. Diachylon ointment is preferably prepared fresh when wanted.

In preparing tar ointment, the tar should be free from granular matter and not incorporated with the mixture of lard and wax until the latter has been cooled to the condition of a smooth, soft ointment. If the tar be added to the hot liquid fats, a granular ointment will result.

Ointments prepared by incorporation of medicinal agents with an appropriate vehicle comprise by far the larger number of official ointments, and practically all those prescribed extemporaneously. The vehicles directed by the Pharmacopœia for the preparation of this class of ointments are lard, benzoinated lard, hydrous wool fat, petrolatum, and simple ointment; when absorption of the ointment is desired, wool fat or its hydrous modification is decidedly to be preferred. All substances to be mechanically incorporated in an ointment must be in the form either of solution or an impalpable powder; the latter condition, in the case of vegetable substances, can be attained only by passing the powder through a fine bolting-cloth sieve (about No. 120 or 150). The incorporation may be effected either in a mortar or on a heavy glass slab by means of a broad spatula, the finely powdered substance being first mixed with a small quantity of the vehicle, and, when a smooth mixture has been obtained, the remainder added; while an ointment slab is, as a rule, preferred in this country, the mortar is used almost exclusively in Europe, and for some ointments is in fact indispensable, particularly when solutions are to be added.

When the quantity of powder to be added is large, it will prove advantageous to melt some of the vehicle and mix this with the powder in a warm mortar before adding the remainder. Some substances can be conveniently brought into a smooth condition by triturating with a little olive or expressed almond oil, such as calomel, lead carbonate, bismuth subnitrate, zinc oxide, etc., as well as certain crystallizable bodies, like mercuric chloride and silver nitrate; for the latter a little oil is decidedly better than water, since upon the gradual evaporation of the latter a return to the crystalline state is probable, giving rise to the presence of minute gritty particles which would cause irritation. Opium should be rubbed smooth with about an equal weight of water, and then at once incorporated with the fatty vehicle before the paste begins to dry. Some salts may be dissolved in water provided they are very soluble as potassium iodide, while others must be reduced to an impalpable condition by trituration, as lead acetate, tartar emetic, zinc sulphate, etc. Red mercuric oxide, iodoform, naphthalene, and boric acid may be triturated with a few drops of alcohol, in a mortar, until rendered impalpable; camphor should be powdered, by the aid of alcohol, just before it is to be used, and added to the ointment after all other ingredients have been incorporated, since it is soluble in the fat and materially softens its

consistence, which, in the case of solid extracts, would interfere considerably with their perfect admixture.

Whenever the extracts of belladonna leaves and of stramonium are to be exhibited in ointments, the pilular extracts should be used, for after having been softened with a small quantity of water or diluted alcohol they are readily incorporated with the fatty vehicle, producing a perfectly smooth mixture free from gritty particles. For the extracts of belladonna leaves and of opium water is to be preferred; but for extract of stramonium diluted alcohol should be used; and in every case an excess of solvent must be avoided, for if the extract be converted into a fluid, it cannot be well mixed with the fat; the consistence of a paste resembling thick honey is best. Another important point in the admixture of solid extracts with ointments is to mix the former with a small portion of the vehicle immediately after they have been softened, and not to allow them to remain on the ointment slab, so as to avoid the drying out of the paste around the edges, which would cause separate particles to appear in the finished product.

Iodine, before admixture with fats, is preferably dissolved in a small quantity of water, with the aid of a little potassium iodide, as it cannot readily be rubbed into a very fine powder by itself; the addition of alcohol is sometimes employed to facilitate division of the iodine, but this plan never yields a satisfactory ointment.

When iodine is ordered in combination with mercurial ointment the addition of potassium iodide is unnecessary, as chemical union will take place between the iodine and mercury; the proper plan would be to rub the iodine to a fine powder and then add a portion of the mercurial ointment, triturating well until the iodine has disappeared and the change of color indicates that union has taken place, after which the remainder of the ointment may be incorporated. If an extract, such as belladonna or stramonium, is also to be added, this should be separately mixed with some of the fat and then added to the previous mixture, whereby a much better ointment will be obtained.

Substances which are wholly or partly soluble in fats, such as menthol, salol, chrysarobin, benzoic and carbolic acids, aristol, naphthol, and the like, should be triturated in fine powder form with a portion of the vehicle liquefied by heat, and, after addition of the remainder, the mixture must be continually stirred until cold. If hydrated chloral, thymol, naphthol, or salol be ordered, together with camphor, in an ointment, the two substances must be triturated together until an oily fluid results, which can then be readily incorporated with the vehicle.

Alkaloidal salts may be incorporated in ointments in solution in water or, if present in large quantity, may be added in the form of a very fine powder; but whenever pure alkaloids are ordered by physicians these should be triturated with a small quantity of warm

oleic acid before they are mixed with the fatty vehicle, as more intimate distribution is thus effected than if the alkaloids be merely rubbed into a smooth paste with olive or almond oil.

Glycerin should never be used in place of oil or water to produce a smooth paste with vegetable or mineral powders, because, although derived from fats, it can be incorporated with them permanently only with difficulty. When glycerin in considerable quantity is ordered to be added to an ointment consisting chiefly of lard or a mixture of lard or oil with wax, the addition of a small proportion of anhydrous wool fat, in place of a like quantity of the regular vehicle, will overcome all difficulty of incorporation. A similar expedient will prove most valuable when large quantities of aqueous fluids are to be incorporated in ointments, or in the case of alcoholic liquids, which ordinarily mix with fats with great difficulty. The pharmacist, in preparing ointments containing fluids, must so combine the constituents that a permanent homogeneous mixture results, from which the fluids will not separate on standing.

It will be found very convenient to keep on hand anhydrous wool fat for the purposes above stated; it is readily prepared by heating some of the commercial lanolin (containing about 30 per cent. of water) on a waterbath until it ceases to lose weight.

When two or more ointments having different fusing points are to be mixed, the firmer should always be rubbed down by itself first, and the softer fats then be incorporated in small quantities at a time, otherwise an imperfect mixture results. A mixture of mercurial ointment with lard or simple ointment offers an example; in cold weather this mode of procedure is all the more imperative; it should also be followed when anhydrous wool fat is to be mixed with softer fats, as the former is usually somewhat tough.

Whenever substances likely to attack metal are ordered in ointments, the incorporation with the fatty vehicle should never be made with steel spatulas, but always with horn or rubber spatulas; the latter can now be had quite pliable, and are admirably adapted for ointments containing salicylic acid, tannic acid, iodine, mercuric chloride, etc.

The Pharmacopœa directs the following 15 ointments to be prepared by incorporation of the medicinal agent with the fatty vehicle:

Latin name.	English name.	Composition.	
Unguentum—			
Acidi Borici	Boric Acid Ointment	Boric Acid	100 Gms.
		Paraffin	50 "
		White Petrolatum	850 "
Acidi Tannici	Tannic Acid Ointment	Tannic Acid	20 "
		Glycerin	20 "
		Ointment	60 "
Belladonnæ	Belladonna Ointment	Extract of Belladonna Leaves	10 "
		Diluted Alcohol	5 mils.
		Hydrous Wool Fat	30 Gms.
		Benzoinated Lard	55 "

Latin name.	English name.	Composition.	
Chrysarobini. .	Chrysarobin Ointment	Chrysarobin	6 Gms.
		Benzoinated Lard . .	94 "
Gallæ . . .	Nutgall Ointment .	Nutgall, in No. 80 Powder	20 "
		Ointment	80 "
Hydrargyri . .	Mercurial Ointment	Mercury	500 "
		Benzoinated Lard . .	250 "
		Prepared Suet . . .	230 "
		Oleate of Mercury . .	20 "
Hydrargyri Ammoniati . .	Ointment of Ammoniated Mercury . .	Ammoniated Mercury .	10 "
		Hydrous Wool Fat . .	40 "
		White Petrolatum . .	50 "
Hydrargyri Dilutum . . .	Diluted Mercurial Ointment (Blue Ointment	Mercurial Ointment .	600 "
		Petrolatum	400 "
Hydrargyri Oxidi Flavi . . .	Ointment of Yellow Oxide of Mercury	Yellow Mercuric Oxide .	10 "
		Water	10 "
		Hydrous Wool Fat . .	40 "
		Petrolatum	40 "
Iodi	Iodine Ointment .	Iodine	4 "
		Potassium Iodide . .	4 "
		Glycerin	12 "
		Benzoinated Lard . .	80 "
Iodoformi . .	Iodoform Ointment .	Iodoform in very fine powder	10 "
		Lard	90 "
Phenolis . . .	Ointment of Phenol (Carbolic Acid Ointment)	Liquefied Phenol . .	2.25 "
		White Petrolatum . .	97.75 "
Stramonii . .	Stramonium Ointment	Extract of Stramonium .	10 "
		Diluted Alcohol . . .	5 mils.
		Hydrous Wool Fat . .	20 Gms.
		Benzoinated Lard . .	65 "
Sulphuris . .	Sulphur Ointment .	Sublimed Sulphur . .	15 "
		Benzoinated Lard . .	85 "
Zinci Oxidi . .	Ointment of Oxide of Zinc	Zinc Oxide	20 "
		Benzoinated Lard . .	80 "

The official directions accompanying each formula and the general directions given above are sufficiently explicit to insure satisfactory ointments, therefore further comment is unnecessary except in two or three cases.

The extinguishment of mercury by means of oleate of mercury, in the preparation of mercurial ointment, is readily effected by trituration in a mortar on a small scale, but large manufacturers probably follow the plan of prolonged agitation in suitable vessels. When the globules of mercury have become invisible, the mixture of lard and suet, melted and partly cooled, is easily incorporated. The Pharmacopœia demands that mercurial ointment, when assayed by dissolving all the fatty matter by means of warm petroleum benzin and weighing the washed and dried residue, shall yield not less than 49 per cent. nor more than 51 per cent. of metallic mercury. In very warm weather mercurial ointment may become almost liquid, and is then liable to lose mercury by separation, hence the necessity for keeping it in a cool place. When mercurial ointment is prescribed in divided doses by physicians, each portion should be separately weighed on paraffin or parchment paper, and then folded as directed in the chapter on Powders.

The present official Blue Ointment (Unguentum Hydrargyri Dilutum, U. S. P.) corresponds in mercurial strength to the preparation formerly known as Mild Mercurial Ointment (Unguentum Hydrargyri Mite) containing nearly one-third (30 per cent.) of its weight of metallic mercury. It should not be used in prescriptions unless specially designated.

In the case of the ointment of yellow mercuric oxide, trituration of the oxide with distilled water is directed for the purpose of insuring reduction to an impalpably fine condition, and the hydrous wool fat facilitates the incorporation of the petrolatum in the presence of the water. Only glass, procelain, or horn utensils should be used, and the ointment should be protected against direct sunlight and high temperatures.

Of the ointments made by chemical action, the official ointment of mercuric nitrate is a striking example. It is made by heating 76 Gms. of lard to a temperature of 45° C. (113° F.), adding 7 Gms. of nitric acid all at once and continuing the heat until the characteristic reaction is complete. Having dissolved 7 Gms. of mercury in 10.5 Gms. of nitic acid, the clear solution is added to the lard mixture, which has been allowed to cool, and the whole thoroughly mixed until cold by means of a porcelain or wooden spatula. When lard is heated and mixed with nitric acid, the former undergoes oxidation at the expense of the acid, olein being converted into a new compound, solid at ordinary temperatures, known as elaidin, the term olein being usually applied to the fluid constituent of fats and fixed oils. The incorporation of the solution of mercuric nitrate subsequently with the elaidin is simply a mechanical admixture, the solution having no chemical effect whatever on the fat. It is essential that the nitric acid be of official strength, and that heat be reapplied, if necessary, to complete the oxidation of the fat; care should be taken that the temperature above indicated be not exceeded, as over a direct fire decomposition of the fat is likely to ensue and a dark brown compound results if too high a heat be applied. The oxidation of the lard goes on quietly, and is known to be ended when effervescence ceases and a soft, solid mass is obtained upon cooling. The solution of mercury in nitric acid can be made in the cold, and may be warmed finally to expel any colored gas that has been retained. If the fat has been properly oxidized and cooled, as directed in the Pharmacopœia, a bright lemon-yellow ointment will result; but if the oxidation of the lard has not been completed before addition of the solution of mercuric nitrate, owing either to the use of weak nitric acid or insufficient heat, decomposition of the metallic salt will result in order to satisfy the avidity of the fat, and the ointment will assume a dark color. Ointment of mercuric nitrate is also known as *citrine ointment* and its official Latin title is *unguentum hydrargyri nitratis*. It should never be brought into contact with metal.

Another instance of chemical reaction in the preparation of oint-

ments is in the original formula for Hebra's ointment: lead oxide is heated with olive oil in the presence of water until all the oxide has chemically combined with the fatty acids derived from decomposition of the oil, the newly formed lead oleate remaining intimately mixed with the excess of oil and the glycerin liberated from the fat. The decomposition taking place will be more fully explained under the head of Saponification, in Part III. The original Hebra's ointment differs from the official diachylon ointment in containing uncombined olive oil and some free glycerin.

The following list gives the titles and composition of the ointments recognized in the *National Formulary:*

Latin name.	English name.	Composition.
Unguentum Calaminæ	Calamine Ointment	Made by incorporating calamine with simple ointment. This ointment is sometimes prescribed as Unguentum Calaminare, and is popularly known as Turner's Cerate.
Unguentum Camphoræ	Camphor Ointment	Made by incorporating camphor with a mixture of lard and white wax. It contains 22 per cent. of camphor.
Unguentum Fuscum	Brown Ointment	Made by melting together camphorated brown plaster, suet, and olive oil. It is popularly known as Mother's Salve, and sometimes prescribed as Unguentum Matris.
Unguentum Hydrargyri Oxidi Rubri	Ointment of Red Mercuric Oxide	Made by triturating red mercuric oxide with water to a perfectly smooth condition and then incorporating it with hydrous wool fat and petrolatum, This ointment is sometimes called for as red precipitate ointment.
Unguentum Picis Compositum	Compound Tar Ointment	Made by adding tincture of benzoin to a previously prepared mixture of yellow wax, lard, and cottonseed oil, continuing the heat until all the alcohol has been dissipated, and then incorporating oil of tar and zinc oxide.
Unguentum Plumbi Iodidi	Ointment of Lead Iodide	Made by incorporating lead iodide in very fine powder with benzoinated lard.
Unguentum Potassii Iodidi	Ointment of Potassium Iodide	Made by dissolving potassium iodide and sodium thiosulphate together in water and incorporating the solution with benzoinated lard.
Unguentum Resorcinolis Compositum	Compound Resorcinol Ointment	Made by rubbing zinc oxide and bismuth subnitrate with petrolatum to a smooth mixture and adding this to a previously melted mixture of yellow wax and anhydrous wool fat; then dissolve resorcinol in glycerin, incorporate this with the warm mixture and add rectified oil of birch. This ointment is sometimes designated as Soothing Ointment.

Latin name.	English name.	Composition.
Unguentum Sulphuris Alkalinum . . .	Alkaline Sulphur Ointment . .	Made by rubbing sublimed sulphur and potassium carbonate with water into a smooth mixture and then gradually incorporating benzoinated lard.
Unguentum Sulphuris Compositum . .	Compound Sulphur Ointment	Made by incorporating sublimed sulphur and precipitated calcium carbonate with a mixture of lard, soft soap, and oil of cade. This ointment is also known as Wilkinson's Ointment and as Hebra's Itch Ointment.
Unguentum Veratrinæ	Veratrine Ointment . . .	Made by triturating veratrine with expressed oil of almond and gradually adding benzoinated lard.
Unguentum Zinci Stearatis	Ointment of Zinc Stearate . .	Made by rubbing zinc stearate in fine powder with white petrolatum.

Two ointments, made with hydrous wool fat or lanolin, are designated as inunctions in the *National Formulary*, thus:

Latin name.	English name.	Composition.
Inunctum Mentholis	Menthol Inunction . . .	Contains menthol and hydrous wool fat.
Inunctum Mentholis Compositum . .	Compound Menthol Inunction	Contains menthol, methyl salicylate and hydrous wool fat.

The *National Formulary* applies the name *Petroxolinum Spissum, Solid Petroxolin* or *Solid Petrox*, to an ointment-like mixture composed of white wax, liquid petrolatum and oil of lavender, held in perfect combination by a soft soap made from oleic acid, stronger ammonia water and alcohol. It may be used as a vehicle for incorporation of various substances, such as iodoform, salicylic acid, sulphur, etc.

A special preparation recognized as *Petroxolinum Hydrargyri, Mercury Petroxolin*, which has the same mercury content as the official diluted mercurial ointment, is directed to be made by triturating mercury with oleic acid and hydrous wool fat until completely extinguished and then incorporating solid petroxolin.

To cleanse the apparatus in or on which ointments have been prepared, the best plan is first to wipe off all remaining grease with clean sawdust or soft paper, and then to wash it well with warm water and lye or soap. In the case of iodoform ointment a few drops of oil of turpentine will remove the characteristic odor readily.

Dispensing of Ointments.—Ointments, cerates, and similar preparations are usually dispensed in glass or porcelain jars with suitable covers (see Fig. 301); if the latter are made of metal or wood, a disk of heavy parchment paper should be inserted, to avoid contact with the fatty substance. Under no circumstances, except when intended for immediate use, should ointments be put up in wooden boxes, as the fat will readily permeate the material. When ointment jars are returned to be refilled, a new jar is preferably substituted for the old one; but if the old one must be used, it should be carefully wiped out

with soft paper and then thoroughly washed with warm lye, rinsed, and dried, before the new ointment is put in; a fresh disk of parchment paper should also be inserted and a new label be put on the jar.

Collapsible tubes are becoming more and more popular as containers for ointments, dermatologic pastes, etc.; they are made of more or less pure block tin and also of celluloid, in different sizes, from ½ to 2 inches in diameter, with openings that are closed with screw caps

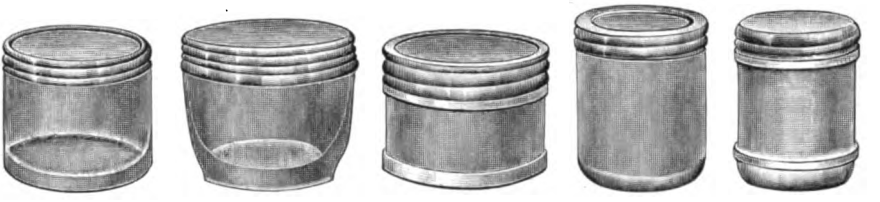


FIG. 301.—Glass dispensing jars for ointments.

(see Fig. 302). Special nozzles, with orifices varying from $\frac{1}{32}$ to ¼ inch in diameter (see Fig. 303), are made to screw on the tube for the application of ointments to the eyes and into the nose or rectum. The more nearly pure the block tin used in the manufacture of collapsible tubes, the more satisfactory are they as containers; celluloid being less pliable is more likely to crack than the tin during the process of expressing the ointment.

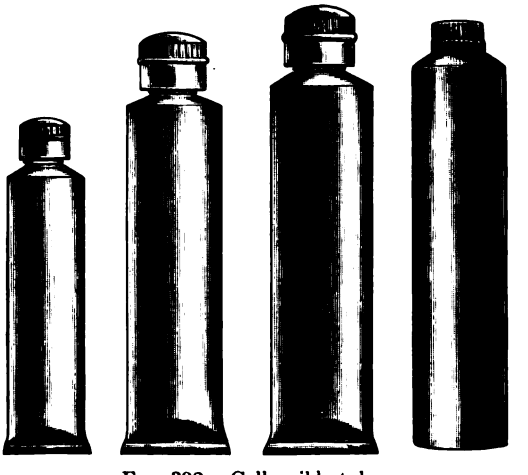


FIG. 302.—Collapsible tubes.

When metallic tubes are used for ointments of mercurials or ointments containing corrosive material, the tubes should be carefully coated on the inside with some pliable resin, such as tolu or benzoin. This may be done by pouring a small quantity of the tincture of either of these balsamic resins into the tube and running it carefully

over the entire inner surface, returning the excess to a special container in which the tincture used for this purpose is kept. Or, if a number of tubes are to be coated at one time, pour from one tube to another until all is used.

Collapsible tubes are usually filled from the bottom, sufficient room being left for folding the ends over at least twice and then clamping them with a pair of broad flat pliers or in large operations by means of special machinery. Various methods have been suggested for filling the tubes, and many of these answer well when large numbers are to be filled. If an ointment is soft enough to pour, or can be softened by heat without injury or danger of separation, the filling of the tubes by pouring the material into them is an easy matter. Care should be used, however, in filling tubes of small diameter by pouring the fused material into them, to avoid closing the tube and preventing the outflow of air. Tubes 1 inch or more in diameter may be very conveniently filled from an ordinary family sausage "stuffer."

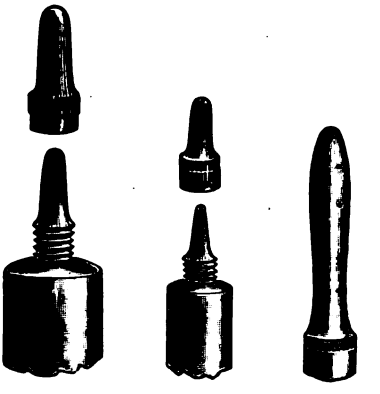


FIG. 303.—Nozzles for collapsible tubes.

Single tubes, and especially small tubes, may be most conveniently filled by using a piece of parchment paper of suitable size. The paper should be rendered thoroughly pliable by dipping it into water, the adhering water being removed by wiping the paper with a towel or piece of gauze. The ointment is then spread on the paper in an oblong mass approximately the size of the tube and wrapped around the ointment by folding the edges together until a cylinder is formed with the paper extending somewhat beyond the ointment and which will easily slide into the tube. This is then dropped into the tube until it reaches the shoulder, when the upper end should be closed by folding or twisting the projecting paper, and held between the fingers and thumb of one hand while the paper cylinder is stripped between the forefinger and thumb of the other hand, in a manner to fill the tube from the shoulder up, while withdrawing the paper as the tube

fills.[1] The great advantage of this plan is shown in the small waste of ointment and the absence of apparatus to be cleaned.

Collapsible tubes should be dispensed in suitable boxes or cartons, with the label bearing directions on the box or carton, for the reason that a label on the tube itself is quickly destroyed by the falling or squeezing of the tube in expelling the ointment. If labels are used at all on the tube they should be long enough to pass entirely around the tube and overlap, otherwise they will not stay in place.

CERATES.

This class of preparations differs from ointments in containing a considerable proportion of wax, and frequently also rosin or oleoresinous substances. Cerates are intended to be applied as dressings, usually spread on linen or soft leather; while they become some what softer at the temperature of the body; they do not liquefy, and are intended to act only locally as protective, cooling, astringent, stimulating, or blistering agents. What has been said before regarding the preparation of ointments by fusion, and also their preservation applies likewise to cerates; owing to their firm consistence the latter are not well adapted to admixture with powdered substances, although fluids are sometimes incorporated with them.

The Pharmacopœia and the *National Formulary* recognize 3 cerates each, which, with the exception of the cerate of lead subacetate, are usually carried in stock by the pharmacist. Three of the cerates contain rosin and in these, yellow wax also is used; hence they will not become rancid. Of the remaining three, one is made of white wax and benzoinated lard, one with white wax, petrolatum, and benzoinated lard, and one with white wax, petrolatum, and wool fat.

The following is a list of the cerates, showing their composition:

Latin name.	English name.	Composition.
Ceratum . . . . U. S. P.	Cerate (Simple Cerate) . .	Contains white wax and benzoinated lard.
Ceratum Camphoræ . Nat. Form.	Camphor Cerate	Contains camphor, liniment, white wax, white petrolatum, and benzoinated lard.
Ceratum Cantharidis U. S. P.	Cantharides Cerate . . .	Contains powdered cantharides, glacial acetic acid, liquid petrolatum, yellow wax, rosin, and lard.
Ceratum Plumbi Subacetatis . . . . Nat. Form.	Cerate of Lead Subacetate (Goulard's Cerate)	Contains solution of lead subacetate, wool fat, white wax, white petrolatum, and camphor.
Ceratum Resinæ . . U. S. P.	Rosin Cerate (Basilicon Ointment) . . .	Contains rosin, yellow wax, and lard.
Ceratum Resinæ Compositum . . . Nat. Form. . .	Compound Rosin Cerate (Deshler's Salve) .	Contains rosin, yellow wax, prepared suet, turpentine, and linseed oil.

[1] This plan was first suggested by Henry P. Hynson in the Section on Practical Pharmacy of the American Pharmaceutical Association.

Camphor cerate and Goulard's cerate both contain 2 per cent. of camphor, which would seem hardly sufficient to impart marked medicinal properties to the preparations.

In the formula for cerate of cantharides the object of macerating the powdered cantharides for 48 hours in a warm place with about half of their weight of a mixture of glacial acetic acid and liquid petrolatum is to facilitate the subsequent solution of cantharidin in the fats, since both liquids are known to exert a solvent effect upon the blistering principle. The official process always insures an efficient blistering cerate, provided the cantharides are of good quality. In order to prevent the separation of the powder from the melted fats, it is important that the mixture, after removal from the waterbath, be constantly stirred until it begins to congeal. In Great Britain Germany, and France this cerate is known as *emplastrum cantharidis* or *emplastrum vesicans;* in some localities it is also designated as *emplastrum lyttæ.*

The official rosin cerate congeals as a perfectly homogeneous mixture upon cooling without stirring, on account of the large proportion of rosin and wax present; stirring of the melted and strained mixture is, in fact, not desirable in this case, as it incorporates considerable air. Rosin cerate gradually grows tougher by age. In cold weather the proportions of lard and yellow wax may be changed with advantage to lard 530 Gms. and yellow wax 120 Gms. in the official formula.

Compound rosin cerate is often called for under the name Deshler's salve. If kept on hand for some time it becomes tough, which condition may be avoided by using olive oil or liquid petrolatum in place of the linseed oil.

DERMATOLOGIC PASTES AND GLYCEROGELATINS.

Of late years ointments and cerates have been largely superseded, especially in Europe, by dermatologic pastes and glycerogelatins The former are ointment-like mixtures of starch, dextrin, or calcium carbonate with glycerin, soft soap, petrolatum, lard, or linseed oil, and medicated by incorporation of ichthyol, salicylic acid, resorcinol, sulphur, zinc oxide, naphthol, etc. They are intended chiefly for antiseptic, astringent, or germicidal effects. As a general vehicle a mixture of equal parts by weight of dextrin, glycerin, and water, commonly designated as *Pasta Dextrinata*, or *Dextrinated Paste*, may be brought into solution with the aid of heat.

The following pastes are recognized in the *National Formulary* and directions given for their preparation:

Latin name.	English name.	Composition.
Pasta Naphtholis . .	Lassar's Naphthol Paste . . .	Made by triturating betanaphthol and precipitated sulphur with petrolatum and then incorporating soft soap with this mixture.

Latin name.	English name.	Composition
Pasta Resorcinolis Fortior	Lassar's Stronger Resorcinol Paste	Made by triturating resorcinol with liquid petrolatum to a smooth thin paste, then incorporating a mixture of resorcinol and starch, and finally adding sufficient liquid petrolatum to make up the required weight. It contains 20 per cent. of resorcinol.
Pasta Resorcinolis Mitis	Lassar's Mild Resorcinol Paste	Made like the preceding preparation, but contains only 10 per cent. of resorcinol.
Pasta Zinci	Lassar's Zinc Paste	Made by incorporating zinc oxide, salicylic acid, and starch with petrolatum.
Pasta Zinci Mollis	Unna's Soft Zinc Paste	Made by incorporating zinc oxide and calcium carbonate with linseed oil and finally adding lime water.
Pasta Zinci Sulphurata	Unna's Sulphurated Zinc Paste	Made by incorporating zinc oxide, precipitated sulphur, and purified siliceous earth with benzoinated lard.

The glycerogelatins are firmer, as a rule, than the pastes, and must be melted before they can be applied to the affected parts, which latter is done by means of a soft brush. The Pharmacopœia recognizes such a preparation as Gelatinum Glycerinatum, Glycerinated Gelatin, composed of equal weights of gelatin and glycerin, which is firm and intended as a vehicle for such substances as chrysarobin, iodoform, resorcinol, etc. Occasionally special mixtures of gelatin, glycerin, and water are used, when softer or even liquid preparations are desired, as gelatin 15 parts, glycerin 45 parts, and water 25 parts, or gelatin 5 parts, glycerin 20 parts, and water 65 parts. The *National Formulary* gives directions for preparing four different glycerogelatins; they are made by mixing the medicinal agent, previously incorporated with glycerin and water, with official glycerinated gelatin, already melted, and finally pouring the homogeneous mixture into suitable containers, where it is allowed to become cold. The proportion of glycerinated gelatin used varies with the different preparations, from 7 to 30 per cent. of the intended weight of the finished product.

The following are the glycerogelatins recognized by the *National Formulary:*

Latin Name.	English Name.	Composition.
Glycerogelatinum Acidi Salicylici	Salicylic Acid Glycerogelatin	Made by triturating very finely powdered salicylic acid with glycerin and water, and adding this mixture to previously melted glycerinated gelatin.
Glycerogelatinum Iodoformi	Iodoform Glycerogelatin	Made by triturating very finely powdered iodoform with glycerin and water and adding this mixture to previously melted glycerinated gelatin.
Glycerogelatinum Zinci Durum	Firm Zinc Glycerogelatin	Made by triturating zinc oxide with glycerin and adding this mixture to a previously prepared mixture of glycerinated gelatin, glycerin, and water.
Glycerogelatinum Zinci Molle	Soft Zinc Glycerogelatin	Made like the preceding preparation, except that less glycerinated gelatin is used, and more glycerin in its place.

PASTE PENCILS.

Another form of modern dermic medication is by means of pencils. These consist of a suitably medicated paste composed of starch 30 parts, dextrin 35 parts, powdered tragacanth 5 parts, sugar 20 parts, and sufficient water to make a firm plastic mass, which is rolled out into rods about 5 millimeters ($\frac{1}{5}$ inch) in diameter and 5 centimeters (2 inches) in length. The pencils are dried at ordinary temperature on parchment paper and wrapped in tin foil. They are sometimes called Unna Pencils, after Dr. Unna, of Germany, who first suggested their use. The *National Formulary* gives directions for preparing Salicylic Acid Pencils, Stili Acidi Salicylici Dilubiles, containing 10 per cent. of salicylic acid, which are made by incorporating 10 parts of the acid with the mass above directed, and then dividing the mixture into pencils of the prescribed dimensions.

CATAPLASMS.

Cataplasms or poultices are wet masses of solid matter, applied to the skin with a view of acting as antiphlogistic or cooling agents and sometimes as counterirritants. Elm, flaxseed, and mustard poultices have long been known as popular household remedies. The *National Formulary* recognizes a clay poultice under the name *Cataplasma Kaolini* or *Cataplasm of Kaolin*, which is intended to be used as an antiseptic cooling dressing. It was formerly official in the Pharmacopœia and is made by mixing finely powdered boric acid with finely powdered kaolin (previously heated on a boiling waterbath for an hour with frequent stirring), then incorporating the mixed powder with glycerin, and finally adding thymol, oil of peppermint, and methyl salicylate. This cataplasm is a stone-colored homogeneous mass, which must be preserved in air-tight containers on account of its tendency to absorb moisture from the air.

CHAPTER XXXIV.

LINIMENTS AND OLEATES.

THESE preparations are closely allied to those described in the preceding chapter, being also intended only for external use.

LINIMENTS.

Liniments are fluid or semifluid preparations, usually in the form of solutions, although in some instances merely mechanical mixtures, the solvent or vehicle being generally a fixed or volatile oil or alcohol, which latter is sometimes mixed with water. Recently the *National Formulary* has introduced a new vehicle under the name Liquid Petroxolin, which is a combination of liquid petrolatum with soft ammonia soap, flavored with oil of lavender; it is a yellowish-brown liquid, capable of being variously medicated by admixture of camphor, chloroform, eucalyptol, iodine, menthol, phenol, tar, etc. When thus medicated, the mixtures or solutions are known as petroxolins of the respective remedial agents. Liniments are applied to the skin with friction, and, when mechanical mixtures only, require to be well agitated before they are applied. For endermatic medication liniments are in many cases to be preferred to ointments, because, being applied with friction, the medicinal agents are more likely to be readily absorbed by the unbroken skin. For this purpose it is essential that the vehicle be of a volatile or fatty character, since non-volatile substances in aqueous solution are either not absorbed at all or only to a slight extent, while the same substances dissolved in alcohol, chloroform or ether are quickly taken up, as shown by their prompt appearance in the secretions.

The Pharmacopœia recognizes 8 liniments and the *National Formulary* 9, of which number 5 are of a fatty nature, 1 is an emulsion of a volatile oil, and 11 are alcoholic or hydro-alcoholic solutions. In addition the *National Formulary* gives directions for the preparation of 16 petroxolins in liquid form.

The following is a list of the liniments recognized in the U. S. Pharmacopœia and *National Formulary*, together with the petroxolins of the latter authority, giving their titles and composition:

Latin name.	English name.	Composition.
Linimentum Aconiti et Chloroformi . . Nat. Form.	Liniment of Aconite and Chloroform . . .	Made by mixing fluidextract of aconite, alcohol, chloroform, and soap liniment.
Linimentum Ammoniæ U. S. P.	Ammonia Liniment (Volatile Liniment, Hartshorn Liniment)	Made by thoroughly agitating sesame oil with ammonia water.

Latin name.	English name.	Composition.
Linimentum Ammonii Iodidi . . . . Nat. Form.	Liniment of Ammonium Iodide	Made by adding ammonia water to a previously made solution of iodine, camphor, oil of lavender and oil of rosemary in alcohol.
Linimentum Belladonnæ . . . . U. S. P.	Belladonna Liniment . . .	Made by dissolving camphor in fluidextract of belladonna root.
Linimentum Calcis . U. S. P.	Lime Liniment (Carron Oil) .	Made by thoroughly agitating linseed oil with lime water.
Linimentum Camphoræ U. S. P.	Camphor Liniment (Camphorated Oil)	Made by dissolving camphor in cottonseed oil.
Linimentum Chloroformi . . . . U. S. P.	Chloroform Liniment . . .	Made by mixing chloroform with soap liniment.
Linimentum Opii Compositum . . . Nat. Form.	Compound Liniment of Opium (Canada Liniment) . . .	Made by thoroughly agitating oil of turpentine with a mixture of albumen and ammonia water, then adding a solution of camphor and oil of peppermint in alcohol, and finally tincture of opium.
Linimentum Saponato-Camphoratum . . Nat. Form.	Camphorated Soap Liniment (Opodeldoc, Solid Opodeldoc) . . .	Made by first preparing a solution of animal soap (sodium stearate), from stearic acid, monohydrated sodium carbonate and alcohol with the aid of heat; after effervescence ceases and the liquid has partially cooled, an alcoholic solution of camphor, oil of rosemary and oil of thyme is added, followed by ammonia water and alcohol.
Linimentum Saponis U. S. P.	Soap Liniment (Liquid Opodeldoc) . .	Made by adding dried soap, granulated or powdered, to an alcoholic solution of camphor and oil of rosemary, together with sufficient water to make up the required volume; the mixture is then agitated until the soap is dissolved, and set aside for 24 hours before it is filtered.
Linimentum Saponis Mollis . . . . U. S. P.	Liniment of Soft Soap (Tincture of Green Soap)	Made by dissolving soft soap in a solution of oil of lavender in alcohol; after 24 hours the liquid is filtered.
Linimentum Saponis Mollis Compositum Nat. Form.	Compound Liniment of Soft Soap . . .	Made by dissolving soft soap in alcohol and adding oil of cade to the solution.
Linimentum Sinapis Compositum . . Nat. Form.	Compound Liniment of Mustard	Made by adding fluidextract of mezereum, oil of mustard and castor oil to an alcoholic solution of camphor.
Linimentum Terebinthinæ . . . . U. S. P.	Turpentine Liniment (Kentish Ointment) .	Made by dissolving rosin cerate in oil of turpentine, with the aid of a gentle heat.
Linimentum Terebinthinæ Aceticum (Linimentum Album) Nat. Form.	Acetic Turpentine Liniment (Stokes' Liniment, St. John Long's Liniment	Made by triturating oil of turpentine and oil of lemon with egg albumen and yolk of egg, and then incorporating acetic acid and rose water.
Linimentum Tiglii . Nat. Form.	Liniment of Croton Oil . .	Made by mixing croton oil, oil of cajuput and alcohol.
Linimentum Tiglii Compositum . . . Nat. Form.	Compound Croton Oil Liniment .	Made by mixing croton oil, oil of sassafras, oil of turpentine and olive oil.

Latin name.	English name.	Composition.
Petroxolinum Betanaphtholis . . . Nat. Form.	Betanaphthol Petroxolin (BetanaphtholPetrox)	Made by dissolving betanaphthol, in fine powder, in liquid petroxolin.
Petroxolinum Cadini Nat. Form.	Cade Petroxolin (Cade Petrox)	Made by mixing oil of cade with liquid petroxolin.
Petroxolinum Chloroformi Camphoratum Nat. Form.	Camphorated Chloroform Petroxolin (Camphor and Chloroform Petrox)	Made by mixing a solution of camphor in chloroform with liquid petroxolin.
Petroxolinum Creosoti Nat. Form.	Creosote Petroxolin (Creosote Petrox) . .	Made by mixing creosote, oleic acid and liquid petroxolin.
Petroxolinum Eucalyptolis . . . . . Nat. Form.	Eucalyptol Petroxolin (Eucalyptol Petrox)	Made by mixing eucalyptol with liquid petroxolin.
Petroxolinum Guaiacolis . . . . . Nat. Form.	Guaiacol Petroxolin (Guaiacol Petrox) . .	Made by mixing guaiacol, oleic acid and liquid petroxolin.
Petroxolinum Iodi . Nat. Form.	Iodine Petroxolin (Iodine Petrox, 10 per cent.)	Made by dissolving iodine and oleic acid in alcohol by agitation, then adding oil of lavender and liquid petrolatum, and after the addition of stronger ammonia water shaking the mixture until a clear solution results.
Petroxolinum Iodi Dilutum . . . . Nat. Form.	Diluted Iodine Petroxolin (Iodine Petrox, 5 per cent.) . .	Made by dissolving iodine in liquid petroxolin.
Petroxolinum Iodoformi . . . . Nat. Form.	Iodoform Petroxolin (Iodoform Petrox) . .	Made by adding eucalyptol, oleic acid and liquid petroxolin to a solution of iodoform in acetone.
PetroxolinumLiquidum (Petrolatum Saponatum Liquidum) . Nat. Form.	Liquid Petroxolin (Liquid Petrox)	Made by warming a mixture of liquid petrolatum, oleic acid, alcohol and stronger ammonia water on a waterbath, with agitation, until clear and then adding oil of lavender.
Petroxolinum Mentholis . . . . Nat. Form.	Menthol Petroxolin (Menthol Petrox) . .	Made by dissolving menthol in liquid petroxolin.
Petroxolinum Methylis Salicylatis . . . Nat. Form.	Methyl Salicylate Petroxolin (Methyl Salicylate Petrox)	Made by mixing methyl salicylate and liquid petroxolin.
Petroxolinum Phenolis Nat. Form.	Phenol Petroxolin (Phenol Petrox)	Made by dissolving phenol in liquid petroxolin.
Petroxolinum Phenolis Camphoratum . . Nat. Form.	Camphorated Phenol Petroxolin (Camphorated Phenol Petrox)	Made by adding a liquefied mixture of camphor and phenol to liquid petroxolin.
Petroxolinum Picis . Nat. Form.	Tar Petroxolin (Tar Petrox) .	Made by mixing oil of tar with liquid petroxolin.
Petroxolinum Sulphuratum . . . . Nat. Form.	Sulphurated Petroxolin (Sulphurated Petrox)	Made by adding oleic acid and a solution of sulphur in linseed oil to liquid petroxolin.
Petroxolinum Sulphuratum Compositum Nat. Form.	Compound Sulphurated Petroxolin Compound Sulphurated Petrox) . .	Made by dissolving thymol and eucalyptol in oil of cade and oil of turpentine, then adding sulphurated petroxolin and finally sufficient liquid petroxolin to bring the mixture up to the required weight.
Petroxolinum Terebinthinæ Venetæ . . Nat. Form.	Venice Turpentine Petroxolin (Venice Turpentine Petrox) . .	Made by mixing Venice turpentine and liquid petroxolin.

SPECIAL REMARKS.

Linimentum Ammoniæ (*Ammonia Liniment*, also known as *Volatile Liniment* and *Hartshorn Liniment*).—Sesame oil has been found superior to cottonseed oil and olive oil for the preparation of this liniment; the resulting product, while thickening somewhat in the course of time, does not separate. The liniment can be quickly made by shaking 1 volume of ammonia water thoroughly with 3 volumes of the oil, partial saponification taking place, which serves to emulsionize the remainder of the oil.

Linimentum Ammonii Iodidi (*Liniment of Ammonium Iodide*).—The addition of ammonia water to the alcoholic solution of iodine, camphor, oil of lavender and oil of rosemary, results in the gradual combination of the iodine with ammonia, producing a colorless solution. As only 4 Gms. of iodine are used in making a liter of the liniment, not more than 4.57 Gms. of ammonium iodide can be formed, and the finished product contains a considerable excess of ammonia.

Linimentum Belladonnæ (*Belladonna Liniment*).—Both the alcohol of the fluidextract of belladonna root and the camphor materially aid absorption of the liniment, and serious results may follow its liberal application. It should never be dispensed except upon a physician's prescription.

Linimentum Calcis (*Lime Liniment*, also known as *Carron Oil*).—The successful preparation of this liniment will depend largely upon the quality of the lime water used; if the latter be of full strength, partial saponification of the linseed oil occurs, which, as in the case of ammonia liniment, serves to emulsionize the remainder of the oil.

Linimentum Camphoræ (*Camphor Liniment*).—The official directions to add the camphor in coarse powder to the cottonseed oil, previously heated, materially facilitates solution, as camphor in lumps dissolves but slowly in oil at ordinary temperature. This liniment is better known as Camphorated Oil.

The Pharmacopœia requires that camphor liniment shall contain not less than 19.5 per cent., nor more than 20.5 per cent. of camphor and directs its determination by means of the polariscope, which at the same time serves to detect the possible use of synthetic camphor, as the latter, which is not officially recognized, is optically inactive. The official method of assay is not within the reach of the average pharmacist, and the following simpler method for determination of the amount of camphor in camphorated oil will be found useful, although it does not differentiate between official or natural camphor and the synthetic article: Heat a given weight of the oil in a tared dish for 90 minutes in an airbath, at a temperature of 110° C. (230° F.); if at the end of that time any odor of camphor persists, the heating must be continued until it has all disappeared. The loss in weight, when multiplied by 100 and divided by the weight of camphorated oil taken for the test, will express the percentage of camphor present.

Linimentum Opii Compositum (*Compound Liniment of Opium*, also known as *Canada Liniment*).—When the oil of turpentine is gradually added to the clear solution of egg albumen in ammonia water, as directed in the *National Formulary*, an excellent emulsion results, which is not changed upon addition of the alcoholic solution of the camphor and oil of peppermint; but when the tincture of opium is finally added, the emulsion takes on a light brown color. No separation has been observed in the liniment after standing for 24 hours.

Linimentum Saponato-Camphoratum (*Camphorated Soap Liniment*).—The first step in making this liniment is the preparation of sodium stearate by reaction between stearic acid and sodium carbonate, which remains in solution in the warm hydro-alcoholic liquid; after addition of the oils, camphor and ammonia water, the mixture solidifies upon cooling, but will soften and melt at the temperature of the body, when applied with friction. The liniment is better known as Solid Opodeldoc.

Linimentum Saponis (*Soap Liniment*, also known as *Liquid Opodeldoc*).—The present official directions differ materially from those of the last Pharmacopœia and appear less desirable. In the author's experience, as good, if not better, results can be obtained in less time, especially if larger quantities of soap liniment are to be made, by mixing the granulated or powdered soap in a dish with about 4 times its weight of hot water and then heating on a waterbath until a clear gelatinous mass results, which is mixed, while still warm, with about two-thirds of the prescribed quantity of alcohol, stirring until perfect solution is effected. The camphor and oil of rosemary having been dissolved in the remainder of the alcohol, are mixed with the soap solution, and enough water is then added to produce the required volume of liniment.

The directions to set the liniment aside for 24 hours, are intended to allow separation of the sodium palmitate always present in Castile soap, which is less soluble and easily removed by filtration.

Linimentum Terebinthinæ (*Turpentine Liniment*, also known as *Kentish's Ointment* or *Kentish Liniment*).—When making this liniment, the rosin cerate should be melted at as low a temperature as possible, so that it does not become too hot, and the oil of turpentine then gradually added with constant stirring, so as to avoid loss by evaporation.

Linimentum Terebinthinæ Aceticum (*Acetic Turpentine Liniment*).—This liniment represents an egg emulsion of oil of turpentine, rendered more efficient as a counterirritant by the addition of acetic acid. As the finished product contains 40 per cent. by volume of oil of turpentine, a better and more permanent emulsion will be obtained if the quantity of yolk of egg directed in the published formula be doubled. After addition of the acetic acid, the liniment gradually becomes whiter and somewhat thicker. The use of oil of lemon appears as a wasteful addition, since its odor is disguised by that of the oil of turpentine. In some parts of the country this liniment is very popular and is generally called for under the name Stokes' Liniment.

The so-called *drying liniments* or *medicated varnishes* consist of mucilage of tragacanth, starch or dextrin, with egg-albumen, suitably medicated, which when applied to the skin leave a thin varnish or protective film, similar to that obtained with collodion.

Olea Infusa (*Infused Oils*).—These are closely allied to liniments, and consist of solutions in oil of the active principles of the drugs from which they are made, together with coloring matter. Usually they are made from alkaloidal drugs, such as belladonna leaves, hyoscyamus, etc., but occasionally also from other drugs, in which case the oil takes up such constituents as may be soluble. The *National Formulary* gives a general process for the preparation of infused oils, primarily intended for Oil of Hyoscyamus, which consists in macerating the powdered drug in a closed vessel for 6 hours with a mixture of alcohol and ammonia water, then adding sesame oil and digesting the mixture, with frequent stirring, at a temperature of between 60° and 70° C. (140° and 158° F.) until the alcohol and ammonia are dissipated, and finally expressing and filtering. 100 Gms. of the finished product are supposed to represent the active virtues of 10 Gms. of the drug, but it is very doubtful whether the oils can take up more than a portion of the alkaloidal principles present in the drug.

Oleum Hyoscyami Compositum or *Compound Oil of Hyoscyamus* of the *National Formulary* consists of a solution of the volatile oils of peppermint, lavender, rosemary and thyme in infused oil of hyoscyamus. This preparation is also known as *balsamum tranquillans*, but is not identical with the *baume tranquille* of the French Pharmacopœia, although resembling it in medicinal properties and to some extent in composition.

Oleum Phenolatum or *Phenolated Oil*, also known as *Oleum Carbolatum* or *Carbolized Oil*, a 5 per cent. solution of phenol (carbolic acid) in olive oil, may be mentioned here, although not belonging to either the infused oils or the liniments. Being applied as a dressing to burns and other sores, it resembles a liquid ointment in character.

Somewhat resembling liniments, although not like these applied by friction, are lotions. The Pharmacopœia does not recognize this class of preparations, but the *National Formulary* gives directions for making four of them, as follows:

Lotio Ammonicalis Camphorata (*Ammoniated Camphor Wash*).—An aqueous solution of sodium chloride, with addition of spirit of camphor and ammonia water. It must be kept in well stoppered bottles and be shaken when it is dispensed. This lotion is also known as *Aqua Sedativa* or *Sedative Water*, and as *Eau Sédative de Raspail.*

Lotio Flava (*Yellow Lotion*).—A mixture of a solution of corrosive mercuric chloride and lime water, resulting in the precipitation of yellow oxide of mercury. It is often prescribed as Aqua Phagedænica Flava, and is popularly known as Yellow Wash.

Lotio Nigra (*Black Lotion*).—A mixture of mild mercurous chloride and lime water, resulting in the precipitation of black mercurous

oxide. This preparation is sometimes prescribed as Aqua Phagedænica Nigra, and is popularly known as Black Wash.

Lotio Plumbi et Opii (*Lotion of Lead and Opium*).—A mixture of an aqueous solution of lead acetate and tincture of opium. A copious precipitate is formed, which must be reincorporated by agitation whenever the lotion is to be used. It is also known as Lead and Opium Wash.

OLEATES.

This class of preparations has been in use by physicians in this country since 1872. Normal oleates are true chemical compounds of oleic acid with metallic oxides or alkaloids, but the oleates medicinally employed are simply mixtures of such normal oleates with oleic acid or some other diluent. The porportion of any particular metallic oxide or alkaloid to be dissolved in oleic acid may vary with the views of the physician; but in the case of normal oleates a certain proportion cannot be exceeded. The expressions 2, 5, 10, or 20 per cent. oleate are used to indicate that 2, 5, 10, or 20 parts of the respective alkaloid or metallic oxide are present in every 100 parts of the finished product. The following table shows the amount of base combined with oleic acid in 100 parts of the respective normal oleates:

Normal Oleate	of Bismuth	22.03	per cent.	of bismuth oxide.
"	of Copper	12.71	"	of cupric oxide.
"	of Iron	8.86	"	of ferric oxide.
"	of Lead	28.98	"	of lead oxide.
"	of Mercury	28.40	"	of mercuric oxide.
"	of Zinc	12.95	"	of zinc oxide.
"	of Aconitine	69.86	"	of aconitine.
"	of Atropine	50.60	"	of atropine.
"	of Cocaine	51.78	"	of cocaine.
"	of Morphine	50.25	"	of morphine (anhydrous).
"	of Quinine	53.44	"	of quinine (anhydrous).
"	of Strychnine	54.21	"	of strychnine.

From these normal oleates weaker preparations can readily be made by admixture with the desired diluent, according to the following rule: multiply the required quantity by the required percentage strength and divide the product by the percentage of the normal oleate; the quotient will indicate the quantity of normal oleate to be used, and subtracting this from the required quantity gives the weight of the diluent necessary.

Solutions of alkaloidal oleates are best prepared by triturating the prescribed quantity of dry alkaloid in a small dish with the necessary weight of oleic acid, and heating the mixture on a water-bath until perfect solution results; they are, as a rule, of 2 per cent. strength, with the exception of morphine and cocaine, usually of 5 per cent. strength, and quinine, frequently prescribed of 25 per cent. strength. At one time it was thought that oleates could produce systemic effects, but numerous experiments have shown this idea

to have been erroneous. Nevertheless they have been found very useful for local medication, both on the skin and by penetration into the skin. Alkaloidal oleates are always liquid preparations, being solutions of the respective normal alkaloids in an excess of oleic acid. The necessary amount of alkaloid and acid for any given weight of solution can be quickly calculated by the rules given on page 134, under Percentage Solutions.

The solution of metallic oxides in oleic acid is effected very slowly even with the aid of heat; hence they are preferably prepared by mutual decomposition, by adding an aqueous solution of the metallic salt to a solution of an alkali oleate. The precipitated metallic oleates are then washed with water to free them from the newly formed alkali salt, preferably with hot water, two or three washings being sufficient; but for mercuric oleate only warm water must be employed, to avoid decomposition. Metallic oleates are usually prepared of normal strength, as they keep better in this form and can be subsequently diluted as wanted. Benzoinated lard or soft paraffins may be employed as diluents when the oleate is intended for epidermatic use, or lanolin when an endermatic effect is desired, as the latter substance is more readily absorbed by the skin.

A solution of castile soap is very often used as the alkali oleate in the preparation of metallic oleates, especially those of lead, copper, and zinc; but since the soap is a sodium oleopalmitate instead of pure sodium oleate, the resulting metallic oleates will also be contaminated with palmitates; in practice, this slight impurity is generally disregarded, and can be reduced to a minimum by allowing the soap solution to stand in a cool place for twenty-four hours and then filtering. The strength of the soap solution generally used is 30 Gms. (or 480 grains) of dry soap to 450 mils. (or Cc.) (or 1 pint) of the solution. Purer metallic oleates can be obtained by using a solution of sodium oleate made directly from oleic acid by the following process: Warm, in a porcelain dish, 28.5 Gms. (or 454 grains) of oleic acid to about 60° or 65° C. (140° or 149° F.) and add slowly 4.5 Gms. (or 71 grains) of sodium hydroxide (90 per cent.) dissolved in a mixture of 18 mils. or Cc. (or 6 fluidrachms) of distilled water and 6 mils. (or Cc.) (or 2 fluidrachms) of alcohol, stirring constantly until the acid is neutralized, which is best ascertained by testing a small portion of the resulting soap, dissolved in alcohol, with a few drops of phenolphthalein solution—not more than a faint pink tint should appear. The soap is next dissolved in sufficient distilled water to produce 450 mils. (or Cc.) (or 16 fluidounces) of solution, and filtered.

The Pharmacopœia recognizes one oleate, namely Oleatum Hydrargyri, Oleate of Mercury, which is a 25 per cent. solution of yellow oxide of mercury in oleic acid, made with the aid of a moderate heat. The addition of alcohol materially facilitates combination of the mercuric oxide with the acid, the heat being continued until all the alcohol has been finally expelled. The official mercuric oleate is of

the consistence of firm butter and should be protected against air and light; all contact with metallic utensils must be carefully avoided.

The oleates of copper, lead and zinc are occasionally called for and can be readily prepared by direct precipitation by adding to 450 mils. (or Cc.) (or 1 pint) of the above-named sodium oleate solution, a solution of the metallic salt, made with distilled water, and containing in 250 mils. (or Cc.) (or 8 fluidounces) respectively, copper sulphate, crystallized, 12.31 Gms. (or 197 grains); lead acetate, crystallized, 18.7 Gms. (or 299 grains); zinc sulphate, crystallized, 14.18 Gms. (or 227 grains).

The *National Formulary* gives directions for the preparation of 5 alkaloidal oleates, all of which are solutions of the normal oleates, either in an excess of oleic acid or in a mixture of oleic acid and olive oil. They are

Oleatum Aconitinæ	Oleate of Aconitine	Containing 2 per cent. of aconitine.
Oleatum Atropinæ	Oleate of Atropine	Containing 2 per cent. of atropine.
Oleatum Cocainæ	Oleate of Cocaine	Containing 5 per cent. of cocaine.
Oleatum Quininæ	Oleate of Quinine	Containing 25 per cent. of quinine.
Oleatum Veratrinæ	Oleate of Veratrine	Containing 2 per cent. of veratrine.

Under the names of ointments of the various oleates, manufacturers have for some time offered a class of preparations in regard to which some confusion exists, as the vehicle as well as the proportion of the oleate used varies with different manufacturers; the vehicle is either benzoinated lard or soft or firm petrolatum, hence the consistence may vary considerably. The term "ointment of any oleate, 5, 10, or 20 per cent.," can have but one meaning as far as the active ingredient is concerned, namely, that the finished product contains 5, 10, or 20 parts of the respective normal oleate in every 100 parts of the ointment, and not 5, 10, or 20 parts of the alkaloid or metallic oxide, as is frequently supposed. Ointments of oleates have received official recognition in two instances, the ointment of mercuric oleate and the ointment of zinc oleate, both of the British Pharmacopœia, the former containing 25 per cent. of normal mercuric oleate and the latter 50 per cent. of normal zinc oleate. Besides these the ointments of aconitine, atropine, and cocaine of the same Pharmacopœia must be looked upon as ointments of oleates, since the respective alkaloids are dissolved in an excess of oleic acid before incorporation with the lard.

CHAPTER XXXV.

PLASTERS AND SUPPOSITORIES.

PLASTERS.

PLASTERS are preparations intended for external application, which, although firmer and more tenacious than cerates, become adhesive by the heat of the body, and may be made to serve the purpose of offering both support and medication to the parts to which they are applied. They are firm solids at ordinary temperature and cannot be spread without the aid of heat, but retain a certain degree of flexibility when applied to the body. The base or mass of nearly all the official plasters is either simple lead plaster or a mixture of the same with wax, rosin, and gum-resins; in large manufactories a rubber mass is specially prepared from caoutchouc and certain aromatic resins and vegetable powders, which is to be preferred in some cases on account of its flexibility and adhesiveness. In the preparation of the rubber plaster base the crude India rubber of commerce is first freed from impurities, by steaming and continuous washing with warm water in suitable machinery until all foreign matter has been removed, after which it is repeatedly passed between heavy steel rollers kept at a temperature of about 35° or 37° C. (95° or 98.6° F.); during this kneading process the rubber gradually softens and assumes a plastic condition which fits it admirably for the incorporation of very finely powdered olibanum, orris root, and rosin or Burgundy pitch, this being also effected between warm smooth rollers.

Some authorities contend that plasters made with a rubber base are wholly inefficient where systemic or even endermatic effects are desired, since, as they claim, the rubber combination does not permit the release and subsequent absorption of the medicinal agent present. Opinions are divided on this point, and while there is no doubt that a volatile or a fatty vehicle will permit the absorption of any medicinal agent in admixture more readily than an insoluble mass of rubber, rosin and wax, or lead oleate, many physicians claim to have observed positive good effects from rubber base plasters, and the testimony of many hundred laymen is in favor of this decidedly more pleasant and convenient form of plasters.

As in the case of ointments, plasters may be divided into three groups with regard to their therapeutic action:

1. Plasters intended to exercise a supportive, protective, antiseptic, counterirritant, or vesicant effect. These will act only epidermatically, and a mass possessing the property of ready and continued adhesive-

ness is to be preferred; hence the official rubber adhesive plaster and similar combinations are well adapted for this group, as they possess the advantage of greater adhesiveness, especially in the presence of moisture.

2. Plasters intended to produce an endermatic effect, such as anodyne, astringent, alterative, sedative, or stimulant. This group includes the official plasters of belladonna and lead; while lead oleate, together with its admixtures of rosin and wax, is preferred by many as a vehicle, it is safe to assume that the large quantities of plasters of this group made with rubber mass are used not without good results.

3. Plasters intended for constitutional and systemic effects. As these require penetration not only into but through the skin, it is absolutely necessary that the vehicle be one of recognized absorbability; for this purpose the modern plaster mulls, also known as salve mulls are now preferred by physicians (see page 509).

The preparation of plaster masses by pharmacists is very similar to that of cerates, being preferably conducted with waterbath heat, those constituents having the highest fusing point being first introduced into the pan or dish, and others of greater fusibility being gradually incorporated. All wholly or partly volatile substances, as oleoresins or essential oils, must be added last, and non-fusible substances must be incorporated in the form of very fine powder whenever possible; as gum-resins are frequently added to plaster mixtures, and as they cannot be reduced to fine powder without injury, they must either be treated in coarse powder with alcohol and the resulting solution of resinous matter then evaporated to a syrupy consistence, as in the case of asafetida, myrrh, and galbanum, or be emulsionized with diluted acetic acid and then evaporated until the liquid hardens on cooling, as in the case of ammoniac. In either case the concentrated liquid should be added to the fused mixture when it begins to cool, the mass being well stirred to insure uniform distribution.

Fluid and solid extracts must be incorporated as in the case of ointments, the former after evaporation to a syrupy consistence, the latter after softening with a little water or diluted alcohol, as the case may be. As in the case of ointments, the extinguishment of metallic mercury in plasters is most conveniently effected by trituration with mercuric oleate.

If any foreign matter, such as sand, pieces of wood, and the like, should be found in the melted plaster, this is best removed by decantation or straining, which must always be done before the insoluble and non-fusible substances are added; if straining be resorted to, it will be advisable to perform this operation with the smallest bulk possible, the strained material being always received in a warm pan or dish.

If plasters are to be preserved for stock, they are usually rolled

into cylindrical pieces of convenient thickness weighing about 4 to 8 oz.; this operation is performed on a slab or board previously moistened with water or expressed oil of almond; these sticks or rolls should be wrapped in waxed or paraffin paper to protect them from the air.

Although, with few exceptions, the term plaster is generally applied to the mass or combination to be spread upon leather or muslin, it is more extensively used in trade to designate the finished spread plaster, ready for application. The spreading of plasters has almost entirely passed out of the hands of pharmacists, hence it does not now appear necessary to describe and illustrate the various appliances which thirty or forty years ago were considered a very essential and important part of every educated pharmacist's outfit. Plaster masses, official and otherwise, can now be purchased of reliable quality spread on muslin or other material, in one- and five-yard rolls, or in definite and convenient sizes, from large manufacturers, and there is today no more reason why a pharmacist should make and spread belladonna plasters than that he should return to the spreading of adhesive plaster, as was done many years ago. Moreover, plasters are prescribed but rarely now by physicians, and, when some new combination is ordered, the pharmacist will probably have little difficulty in spreading a fair quality and appearance by following the few general directions here given.

For extemporaneously spread plasters the best material is soft white leather, the kind known in the trade as plaster skin. A piece should be cut 1 inch larger each way than the size of the plaster ordered; thus a 4 x 6 plaster would require a piece of leather 5 x 7 inches; now prepare 4 strips, ½ inch in width, of stiff paper, preferably glazed, and having previously prepared the plaster mass on a water-bath, as directed above, apply the paper strips to the rough side of the plaster skin in such a manner that the desired space shall remain uncovered, and carefully pour the melted plaster on the leather, smoothing the surface with a warm spatula, or by holding the spread plaster near a stove or furnace register and allowing the soft material to run smooth. Then, having placed the spread plaster on a level surface, with a quick motion remove the paper strips before the plaster surface hardens, so that a clean half-inch margin around the plaster proper may be obtained. In place of a spatula, the roller shown in Fig. 304 may be used with advantage for smoothing the spread plaster mass; it should be dipped in hot water, so as to become warm, before it is used, and then be moistened with a mixture of 1 volume of glycerin and 2 volumes of water to prevent adhesion.

If the paper strips be attached before the melted mass is ready to be applied, the paste is likely to dry out, when subsequent removal of the paper from the rough leather becomes difficult, and hence some pharmacists prefer to moisten the strips with a damp sponge

just previous to spreading the plaster mass; this plan has been found very advantageous. Instead of using paper strips, some prefer to cut a frame of thin cardboard, with a central opening of the required shape and size of the plaster, which is tacked down on the plaster skin. The amount of material necessary for spreading a plaster of the required thickness need not exceed 12 to 15 grains for each square inch, or about 0.165 Gm. for each square centimeter. Plaster spreading requires manipulative skill, and practice alone can bring success; yet the writer has seen some plasters spread by students in his laboratory, who had never before seen the operation, that would have been a credit to any first-class pharmacy.

Mammary or breast plasters are always made circular in form, about 8 inches in diameter, with a 1-inch margin; a hole $1\frac{1}{2}$ inches in diameter is cut in the centre, and from this point to the outer edge the plaster is slit to admit folding over the breast. Such plasters are preferably spread on chamois skin, which is softer.

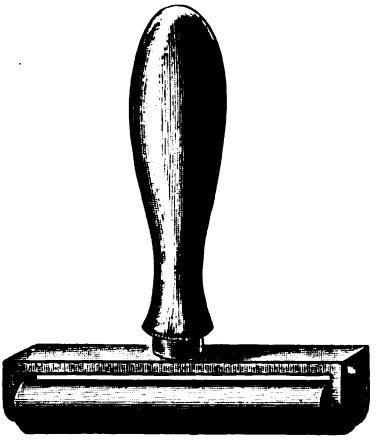


FIG. 304.—Plaster roller.

Fly plaster is the name frequently applied to cantharides or blistering cerate when the same has been spread upon adhesive plaster ready for use. The spreading of the cerate is done in the manner already outlined for regular plaster masses, except that heat is unnecessary, since the cerate is sufficiently soft to permit of being spread by simple pressure of a spatula; in cold weather the spatula may be slightly warmed with advantage. The amount of blistering cerate necessary for a given space should not exceed 10 to 12 grains for each square inch, or about 0.120 Gm. for each square centimeter. As fly plasters are not intended for prolonged application, ordinary muslin or adhesive plaster will answer on which to spread the cerate, the latter material being preferable on account of the adhesive edges, which serve to keep the plaster from slipping. A piece of tarletan, a trifle larger than the surface of the cerate, should be firmly pressed over the same, which, while not interfering with the blistering action of the cantharides, protects the skin from being much soiled, and prevents any of the cerate from getting under the skin if the blistered surface should be lacerated by sudden removal of the plaster.

Porous plasters, which have become very popular, differ from ordinary spread plasters in having numerous small holes punched

through them, rendering them more comfortable for prolonged application, by allowing exhalations of the skin to pass off freely. They are prepared on an extensive scale by special machinery.

The Pharmacopœia recognizes 4 spread plasters, and 3 plaster masses; of the latter class the *National Formulary* also directs the preparation of 2. Very few of these are used by physicians at the present time, except adhesive plaster for surgical purposes and belladonna plaster for its anodyne effect; spread plasters, however, are still a very popular mode of medication, and enormous numbers of machine-spread plasters are annually sold. The official directions for preparing the various plasters are explicit, requiring little or no additional remarks; with care and observance of the precautions before stated, good results will be obtained.

Lead plaster is, strictly speaking, a chemical compound—lead oleate or lead soap—the manufacture of which will be more fully explained in connection with the subject of saponification. It enters either directly or indirectly into the composition of many plasters.

The following is a list of plasters recognized in the U. S. Pharmacopœia and the *National Formulary:*

Plaster Masses.

Latin name.	English name.	Composition.
Emplastrum Belladonnæ . . . . U. S. P.	Belladonna Plaster	Consists of a mixture of extract of belladonna leaves and either rosin adhesive plaster or rubber adhesive plaster.
Emplastrum Elasticum U. S. P.	Rubber Plaster (Rubber Adhesive Plaster) .	Consists of a mixture of rubber, resins and waxes, with a filler of an absorbent powder, such as orris root or starch, mechanically mixed. It occurs also spread upon cotton cloth or other fabric.
Emplastrum Fuscum Camphoratum . . Nat. Form.	Camphorated Brown Plaster (Camphorated Mother Plaster)	Consists of a mass obtained by boiling red oxide of lead and olive oil together until the red color has turned brown and the mixture has assumed a suitable consistence, yellow wax and camphor. It is sometimes designated as Emplastrum Matris Camphoratum.
Emplastrum Plumbi U. S. P.	Lead Plaster (Diachylon Plaster)	Consists of lead oleate, obtained by boiling a mixture of lead oxide, olive oil, lard and water, until saponification is complete, and a homogeneous, pliable and tenacious mass results; the liberated glycerin is removed by repeatedly washing the mass with warm water.
Emplastrum Resinæ . U. S. P.	Rosin Plaster (Rosin Adhesive Plaster, Adhesive Plaster) .	Consists of a mixture of lead plaster, rosin, and yellow wax.
Emplastrum Saponis Nat. Form.	Soap Plaster .	Consists of a mixture of lead plaster and soap.

Spread Plasters.

Latin name.	English name.	Composition.
Emplastrum Cantharidis U. S. P.	Cantharides Plaster	Made by spreading cantharides cerate upon rosin adhesive plaster, each square centimeter containing 0.1 Gm. of the cerate.
Emplastrum Capsici U. S. P.	Capsicum Plaster	Made by applying a thin even coating of oleoresin of capsicum to the surface of rubber adhesive plaster. Fifteen square centimeters of the spread plaster contain 0.25 Gm. of the oleoresin.
Emplastrum Sinapis (Charta Sinapis) U. S. P.	Mustard Plaster (Mustard Paper)	Made by spreading a mixture of deoleated black mustard and a solution of rubber, on paper, cotton cloth or other fabric. Twenty square centimeters of the spread plaster contain 0.5 Gm. of the deoleated mustard.

SPECIAL REMARKS.

Emplastrum Belladonnæ (*Belladonna Plaster*).—While the preparation of belladonna plaster presents no difficulty, it is essential that the extract of belladonna used be of full official strength, since the Pharmacopœia requires that the plaster, when assayed by the official method, shall yield not less than 0.35 nor more than 0.40 per cent. of mydriatic alkaloids. The Pharmacopœia also demands that all machine-spread belladonna plasters shall conform to the above standard of alkaloidal strength when tested by the official method of assay. In view of the variability in quality of the commercial belladonna plasters, the official requirement appears very desirable.

Emplastrum Capsici (*Capsicum Plaster*).—The body of the plaster consists of the official rubber plaster spread on fabric, the surface being brushed over with oleoresin of capsicum, 0.25 Gm. of the latter being contained in every 15 square centimeters, or about 1.9 grains in every square inch.

Emplastrum Elasticum (*Rubber Plaster.*)—The official plaster, also known as Rubber Adhesive Plaster, consists of a rubber plaster mass, prepared as explained on page 503, and spread on suitable fabric.

Rubber adhesive plaster has almost entirely replaced the ordinary or rosin adhesive plaster, as it is more permanent and can be applied without the aid of heat, but it is apt to prove somewhat irritating when kept in contact with the skin for some time. Manufacturers of this plaster now prefer to incorporate zinc oxide with the rubber mass before it is spread on muslin or other material, and apply the name *zinc oxide adhesive plaster* to the spread product. Such an improved rubber plaster is known as *Collemplastrum Zinci* in the German Pharmacopœia.

Emplastrum Plumbi (*Lead Plaster*, also known as *Diachylon Plaster*).—The official process of boiling a mixture of olive oil and melted lard

with finely powdered lead oxide in the presence of water, results in a chemical reaction known as saponification, whereby the oxide unites with fatty acids of the lard and oil, glycerin being liberated at the same time and subsequently removed by washing with warm water. The presence of water is essential to facilitate reaction between the lead oxide and the fats, and to prevent an undue rise of temperature; boiling water must be added from time to time, as it evaporates, and the mixture must be kept continually boiling until a pliable and tenacious mass is obtained. The mass is finally freed from water by kneading on a warm slab, and is then rolled into cylindrical shaped pieces and wrapped in paraffin paper to protect it against the action of the air.

The official lead plaster is a mixture of lead oleate, palmitate, and stearate.

Emplastrum Sinapis (*Mustard Plaster*, also known as *Mustard Paper* and *Mustard Leaf*).—Since mustard contains considerable fixed oil, this must first be removed by treating the ground seed with petroleum benzin, after which the deoleated powder is mixed with a solution of rubber in benzin to the consistence of a thick magma, and then applied to one side of well sized cloth or paper, and allowed to dry. The official plaster contains in 100 square centimeters not less than 2.5 Gms. of black mustard deprived of its fat, which is equivalent to about 10 grains in a space of 4 square inches.

Plaster Mulls.—European dermatologists some years ago introduced a class of preparations known as *plaster mulls*, which are intermediate in consistence between plasters and cerates. These plaster mulls, also called salve mulls, are especially indicated in cases in which prolonged application is necessary, since, owing to the porous character of the mull or gauze employed, they permit ready evaporation, and thus prevent maceration of the epidermis, which is likely to occur in the case of more occlusive dressings. They are sometimes prescribed as steatins and spread ointments; thus, *steatinum zinci salicylatum*, *unguentum hydrargyri extensum*, etc. The best vehicle for these plaster mulls or salve mulls is a mixture of suet and lard, usually benzoinated, to which wax or lead plaster is occasionally added to give more firmness; it is easily spread when warmed, but does not melt when applied to the body. While plaster mulls or salve mulls are, as a rule, produced on a large scale more conveniently with the aid of special apparatus, so devised that the melted mass is allowed to run slowly and smoothly over suitable material in such a manner as to insure uniform spreading, they can also be made by the pharmacist in the following manner: A piece of mull or gauze is evenly stretched upon a piece of parchment paper, previously moistened with water and wiped off with a cloth; it is held in position by means of thumb tacks, and the medicated mass, previously melted and partly cooled, is then spread evenly over the gauze by means of a broad, flat brush, the surface being made smooth with the aid of spatulas, which have been dipped in hot water

and wiped dry. Finally, the plaster mull is withdrawn carefully from the parchment paper, suspended on a string in a cool room, and when perfectly cold covered with paraffin paper and rolled up. These plaster mulls should be preserved in a cool, dry place. The *National Formulary* applies the name salve mulls only to these preparations and gives the composition of the following:

LIST OF SALVE MULLS OF THE NATIONAL FORMULARY.

Latin name.	English name.	Composition.
Mulla Creosoti Salicylata (Unguentum Creosoti Salicylatum Extensum) . . .	Salicylated Creosote Mull	Made from yellow wax, benzoinated suet, salicylic acid, and creosote.
Mulla Hydrargyri Chloridi Corrosivi (Unguentum Hydrargyri Chloridi Corrosivi Extensum) .	Corrosive Mercuric Chloride Mull . . .	Made from benzoinated lard, benzoinated suet, and an alcoholic solution of corrosive mercuric chloride.
Mulla Acidi Salicylici (Unguentum Salicylatum Extensum) .	Salicylic Acid Mull . . .	Made from benzoinated lard, benzoinated suet and salicylic acid.
Mulla Zinci (Unguentum Zinci Extensum)	Zinc Mull . .	Made from benzoinated lard, benzoinated suet and zinc oxide.

SUPPOSITORIES.

Suppositories are solid, medicinal preparations designed to be introduced into the rectum, vagina, urethra, or nose; when intended for the two last named they are usually termed bougies. They are of such consistence that, while retaining their shape at ordinary temperatures, they will slowly melt at that of the body or liquefy in the presence of moisture. The usual shape of rectal suppositories is that of a cone with a rounded apex (see Figs. 305 and 306), but the difficulty of readily introducing these into the rectum, on account of the resistance offered by contraction of the sphincter muscle, led to the suggestion of a new shape by H. S. Wellcome, of London (1893), as shown in Fig. 307, the great advantages of which become apparent when it is remembered that the bulbous end is inserted into the rectum first, and that as soon as the greatest diameter, which is about one-half inch from the point, has been passed, expulsion of the suppository is impossible, by reason of the very contractile force of the sphincter, which renders retention of the ordinary conical shape often so difficult.

Vaginal suppositories are made either globular or similar to rectal suppositories, as shown in Fig. 308, while, for urethral and nasal bougies the pencil shape, seen in Figs. 309, 310, and 311, has been adopted, the last named being about one-third as long, but twice as thick as the urethral bougies.

Suppositories are intended to insure a slow and uniform diffusion of their medicinal constituents to those internal parts to which they may be applied, and the choice of vehicle is made accordingly. The

best substance for the preparation of suppositories is undoubtedly cacao butter, or oil of theobroma, first suggested in 1850 by the late

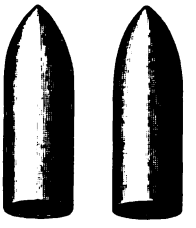


FIG. 305.—Rectal suppositories (for adults).

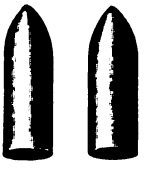


FIG. 306.—Rectal suppositories (for children).

FIG. 307.—The Wellcome-shape suppository.

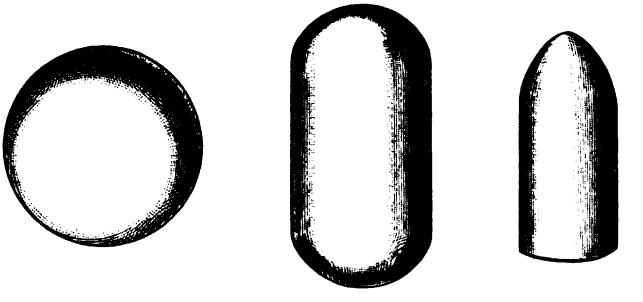


FIG. 308.—Vaginal suppositories.

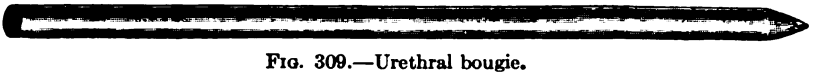


FIG. 309.—Urethral bougie.

FIG. 310.—The Wellcome-shape urethral bougie.

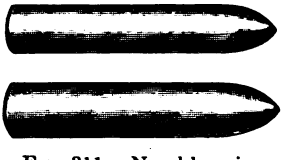


FIG. 311.—Nasal bougies.

A. B. Taylor, on account of its low fusing point and bland, non-irritating properties. When medicinal agents, such as volatile oils, and the like, which have a softening effect on the fatty vehicle, are

ordered in suppositories, and likewise during the summer season, and in warm countries, it will frequently be found impossible to make suppositories with a cacao butter basis without the addition of spermaceti, which latter may be used to the extent of 5, 10, or even 15 per cent. of the weight of the fat, but the melting point of the mixture must not be allowed to rise above 37° C. (98.6° F.). Wax has also been suggested but is inferior to spermaceti and should be used in smaller quantity, as it has a tendency to harden. At the same time it must be borne in mind that the presence of a considerable quantity of insoluble matter, vegetable or mineral powders, has the tendency to raise the melting point of the fat; in some instances the difference has been observed to be as much as 5° or 6° C. (9° to 14.4° F.). A mixture of glycerin and gelatin, known as glycerin jelly, is frequently employed for vaginal suppositories and nasal and urethral bougies, on account of its ready miscibility with water. It is admirably adapted for the exhibition of solid extracts, as those of opium, belladonna, and ergot, and such substances as boric acid, hydrated chloral, iodine, iodoform, alkali bromides and iodides, ichthyol, etc. Tannic acid and alum, considered incompatible with gelatin, can nevertheless be made into satisfactory suppositories or bougies with glycerin jelly by the modified process given below. The porportions best adapted for general purposes are gelatin 20 parts, glycerin 40 parts, and water 80 parts, the whole to be reduced by evaporation to 100 parts. For some purposes these proportions may have to be changed; thus, for hygroscopic drugs, such as potassium or sodium iodide and bromide, hydrated chloral, etc., a mixture of gelatin 10 parts, water 40 parts, and glycerin 15 parts, evaporated to 25 parts, will be found much better. For vaginal suppositories and urethral bougies intended to be medicated with zinc sulphate, cupric sulphate, silver nitrate, extract of opium, corrosive mercuric chloride, etc., a mixture of gelatin 10 parts, glycerin 30 parts, and water 40 parts, evaporated to 60 parts, will be found more desirable; while for bougies and suppositories of all kinds, containing large proportions of powdered drugs insoluble in water or alcohol, a softer mass, composed of gelatin 30 parts, glycerin 15 parts, and water 120 parts, evaporated to 104 parts, is to be preferred. Glycerin jelly is prepared by soaking the gelatin in the water for a few hours, or overnight, in a covered dish, then adding the glycerin and evaporating on a waterbath to the required weight.

Suppositories and bougies of alum or tannic acid with glycerin jelly are best made with a weak solution of gelatin as follows: macerate 5 parts of gelatin with 35 parts of water, add 10 parts of glycerin, heat on a waterbath until solution is effected, and evaporate to 40 parts. To the warm mass add a hot solution of 8 parts of alum in 25 parts of water. This addition causes the gelatin to coagulate, but, on continuing the heating of the mass, it again becomes liquid. Finally, evaporate the whole to 40 parts and pour into chilled moulds. For tannin bougies, proceed exactly as in the case of alum bougies, using

1 part of tannic acid dissolved in 5 parts of glycerin in place of the hot alum solution.

The official glycerinated gelatin (Gelatinum Glycerinatum, U. S. P.) is prepared by pouring sufficient sterilized water over 100 Gms. of gelatin to cover the same, and allowing to stand for 1 hour; the water is poured off and the gelatin allowed to drain for a few minutes and transferred to a tared dish. After the addition of 100 Gms. of glycerin the mixture is heated on a waterbath until the gelatin is dissolved; the solution, while hot, is strained and the heat continued until the product weighs 200 Gms. It is too firm for use by itself as a vehicle for suppositories, and hence the Pharmacopœia directs that the medicinal agent shall be mixed with a little water and sufficient glycerin to make the weight of the mixture one-half that of the proposed finished mass, after which it is thoroughly incorporated with an equal weight of glycerinated gelatin previously melted on a waterbath.

The Pharmacopœia recommends that rectal suppositories made with cacao butter should weigh about 2 Gms. (30 grains). Urethral bougies should be either 7 or 14 centimeters (2.8 or 5.6 inches) in length and weigh about 2 or 4 Gms. (30 or 60 grains) if made with glycerinated gelatin; if made with cacao butter, they should weigh about one-half as much. Vaginal suppositories should weigh about 4 Gms. (60 grains) if made with cacao butter, or 10 Gms. (150 grains) if made with glycerinated gelatin.

Since suppositories are, like ointments, simply mechanical admixtures of the medicinal constituents and a vehicle, the former must always be incorporated in the form of an impalpable powder or in a state of solution, solid extracts being rubbed into a smooth paste with water. On account of the peculiar application of suppositories, it is important that no coarse or gritty particles should ever be contained therein. They are made either entirely by hand, by casting in appropriate moulds, or by cold compression in suitable apparatus.

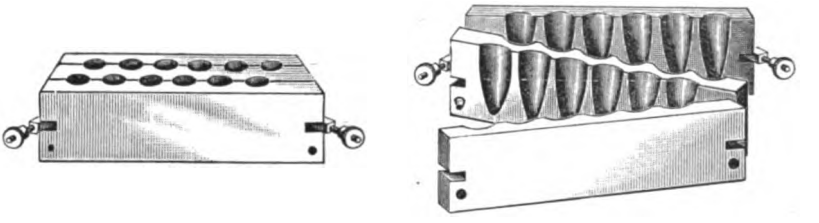
Hand-made suppositories are, as a rule, not so exact and uniform in shape as those moulded, although some pharmacists have attained considerable perfection and dexterity in following this convenient method. The usual plan is to effect an intimate mixture of the active ingredients and vehicle in a mortar, by forming them into a uniform mass, and transfer the mass to a graduated tile to be divided into the required number of equal parts, which are then properly shaped with the fingers. To prevent adhesion of the mass to the tile or fingers, it may be dusted with finely powdered starch or a mixture of starch and lycopodium. The method, of course, excludes the use of glycerin jelly, and, if the mass shows a disposition to crumble, the addition of a few drops of castor oil will overcome the difficulty, rendering the mass plastic. One of the best vehicles for making suppositories by hand, or by cold compression, is a mixture of cacao butter 5 parts, castor oil 1 part, and yellow wax 1 part, which fuses at about the same temperature as cacao butter; another mixture melting at body temperature

is composed of cacao butter 2 parts, hydrous wool fat and white wax, of each 1 part.

For casting suppositories in moulds it is necessary to have the mass in a fluid state. If carefully and skilfully followed, this method yields the most perfectly shaped and finished suppositories that can be made; but it requires practice to insure success, presenting more difficulties than any other method. If the fluid mass be poured into the moulds too warm, immediate separation of the insoluble ingredients occurs, which settle in the apex of the cone. If allowed to cool too fast, it will not flow properly, and fill the moulds imperfectly; the proper condition of the mass is reached when the fluid is of a thin, syrupy consistence and a slight film begins to form on the surface. High heat should be avoided in preparing the mass, a low waterbath heat being amply sufficient for melting the cacao butter or glycerin jelly. Any solid extract to be added should be softened on a slab or pill tile with a little water, mixed with about one-third of the melted vehicle, and transferred to the dish or capsule containing the remainder of the melted vehicle, which has been removed from the waterbath and allowed to cool somewhat. By stirring with a glass rod or narrow steel spatula the extract will become uniformly incorporated, after which any solid ingredient, in impalpable powder, may be added and thoroughly mixed; the fluid mass is then immediately poured into well chilled moulds, with constant stirring to prevent separation. It is important that no heat be applied to the melted mass after the addition of the medicinal constituents lest separation occur, particularly in the case of extracts, which cannot afterward be successfully overcome. If perchance the mixture solidifies before it is transferred to the mould, it may again be liquefied by holding the dish or capsule over the steam arising from a hot waterbath and stirring assiduously. The moulds must be perfectly clean and dry, having been previously well chilled by placing them on ice; there will then be no occasion whatever for dusting them with lycopodium or other substance. If the fluid mass is of the right consistence and the mould cold, it will immediately congeal and contract on being poured into the moulds, but sufficient time should be allowed for the suppository to harden throughout, otherwise trouble may be experienced in removing them; in winter thirty minutes, as a rule, will suffice, whereas forty minutes or an hour may be necessary in summer, unless the mould, after having been filled, be placed in an ice-chest. Various styles of moulds are in use among pharmacists, those known as divided moulds, opening either horizontally or vertically, being preferred on account of the convenience with which they can be taken apart and cleaned. Figs. 312, 313, 314, and 315 represent four different styles of moulds, from all of which the suppositories can be quickly removed by bearing slightly with the finger against the conical ends after the moulds have been opened.

Fig. 316 represents a large brass-hinged mould in which four dozen

suppositories can be cast at one time; it is made by the F. J. Stokes Machine Co., of Philadelphia, Pa.



Closed. Open.

FIG. 312.—Maris' suppository mould.

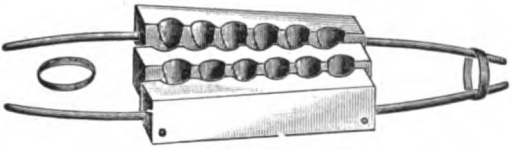


FIG. 313.—Wirz's suppository mould (open).

FIG. 314.—Blackman's suppository mould.

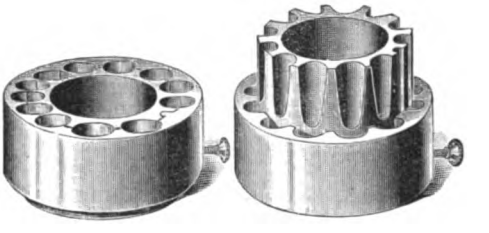


FIG. 315.—See's suppository mould.

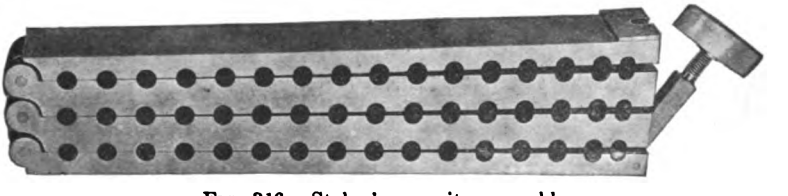


FIG. 316.—Stokes' suppository mould.

The following medicated suppositories have at times proved troublesome, probably for want of proper understanding of the conditions present:

Suppositories of Trional and Trional and Codeine.—Suppositories of trional and trional and codeine are extensively used in some localities,

especially in hospitals. Trional is soluble in hot cacao butter, but upon cooling the solution rapidly solidifies into an unmanageable mass. The best plan of incorporating the trional is to rub it up into an impalpable powder, mix it with castor oil into a smooth paste, 5 minims of oil for 20 grains of trional, and then add this to the melted cacao butter, previously cooled to about 43° C. (109.4° F.); the mixture is well stirred and poured into moulds. If codeine is to be used together with trional, it may be dissolved directly in the melted fat; but as solution takes place slowly, it is better to dissolve the alkaloid in a little alcohol and add the solution to the warm fat, when the alcohol will be dissipated; the trional is added in the manner directed above.

Suppositories of Hydrated Chloral.—If these are to be made with glycerin jelly, little or no difficulty is experienced, nor with cacao butter if the proportion of hydrated chloral is small (10 or 15 per cent.). Hydrated chloral will liquefy cacao butter if added in large quantity, and yet with the aid of a little castor oil, 5 minims for 15 grains of powdered hydrated chloral, a paste is obtained which, according to H. B. Dunning, when mixed with 15 grains of melted and cooled cacao butter, produces firm and satisfactory suppositories, containing 50 per cent. of the medicinal agent. Such suppositories should always be kept in a cool place during warm weather. P. MacEwan recommends in *Art of Dispensing* the following plan for suppositories containing 60 per cent. of hydrated chloral: Melt 60 grains of white wax (shredded) in a wide-mouth vial on a waterbath, add 180 grains of powdered hydrated chloral, shake well, and add 60 grains of cacao butter previously melted. Continue to shake until creamy and pour into chilled moulds.

Suppositories of Tannic Acid and Extract of Belladonna.—Tannic acid, powdered nutgall, and similar astringent substances are likely to cause trouble with extract of belladonna or other alkaloidal drugs, and even without such extracts will cake if the cacao butter has a temperature above 54° C. (129.2° F.). The cold compression method is to be preferred for all such combinations. If the suppositories are to be cast in moulds, the proper plan is to soften the extract with the smallest possible amount of water and mix it with about one-third of the melted cacao butter at a temperature between 38° and 43° C. (100.4° and 109.4° F.), using another third of the melted fat for incorporation of the finely powdered astringent. Finally, add both mixtures to the remaining fat, mix well, and pour at once into well chilled moulds.

Suppositories of Iodoform.—Iodoform should never be mixed with melted cacao butter while the latter is hot; and if balsam of Peru is also to form part of the suppositories, it should be mixed into a smooth paste with the iodoform, which is then incorporated with about one-half of the melted cacao butter containing 10 per cent. of wax, and when thoroughly mixed, transferred to the dish containing the remainder of the fatty base, well stirred and poured into moulds.

The numerous difficulties attending the casting process have led many pharmacists to abandon this process in favor of cold compression. The chief advantages of the compression method are the saving of time and the absence of all danger of overheating and of separation of extracts and other ingredients, while the suppositories are uniform in composition and leave nothing to be desired in appearance, although the finish is possibly not quite so perfect as in carefully cast suppositories. The mass for compression is prepared in a mortar, as for hand-made suppositories, and, when a uniform mixture has been obtained, it is removed and cut up into small pieces, which are placed in a hopper or barrel of the compressor.

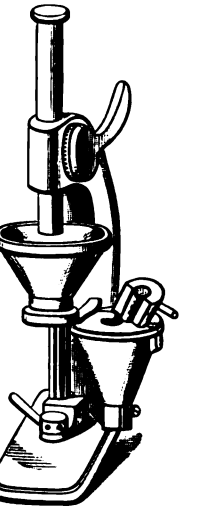
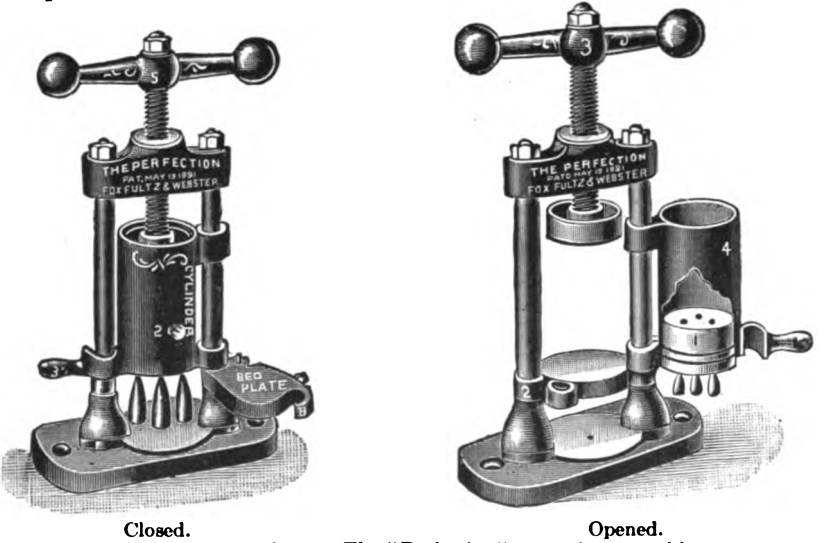


FIG. 317.—The Archibald suppository machine.

The first successful compression mould for dispensing purposes was that known as the Archibald mould (see Fig. 317), which is still used by some. The only objection to this mould is the tedious removal of the finished suppository; the adhesion of the mass to the sides can be readily overcome, however, by swabbing the mould with a pledget of cotton dampened with glycerin between every two compressions.



Closed. Opened.

FIGS. 318 and 319.—The "Perfection" suppository machine.

The four apparatus shown in Figs. 318, 319, 320, and 322 are improvements on the Archibald mould in so far that 3 rectal supposi-

tories can be compressed at once, while the finished product is easily and quickly removed. They differ from each other only in the position of the compressor, two being perpendicular and the other horizontal; all, however, require considerable effort to force the mass through the small openings in the top of the moulds into the moulds proper underneath, which is the only objection that can be urged against them. It sometimes happens that the mould becomes "fixed" in the cylinder of the "Perfection," Freck, and other suppository compressing machines, in which case it can easily be loosened by means of the device shown in Fig. 321, and known as a mould starter. Each of the 4 compression machines is provided with a set of 3 suppository moulds (2 rectal, 30 and 15 grains, and 1 vaginal) and 1 bougie mould. In the Archibald machine the moulds are placed in a swinging bed, which is secured under the cylinder by means of a lever, and after the suppository has been compressed the swinging bed is loosened, the mould taken out and opened, and the suppository removed by gently pushing it with the thumb. In the 3

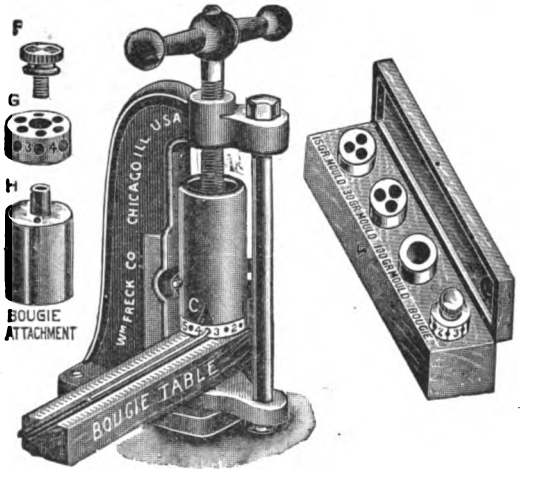


FIG. 320.—Freck's suppository machine with bougie attachment, graduated bougie table, mould box, and pipe attachment.

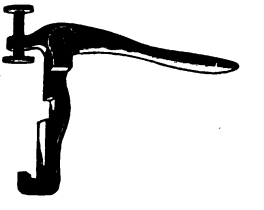


FIG. 321.—Mould starter.

other machines the moulds are screwed into the lower part of the cylinder, or slipped into the cylinder from the top, and rest firmly against an iron bed-plate. To remove the compressed suppository it is only necessary to open the bed-plate, as shown in Fig. 318, and, by one or two turns of a screw, push the suppositories out of the moulds. For the compression of nasal or urethral bougies a plate is put into the cylinder and a tube attached, through which the mass can be forced to any desired length.[1]

Bougies, made with glycerin jelly, are cast in special moulds, such

[1] The Genese suppository machine and compressor, which were illustrated and described on pages 396, 397, and 399, of the first edition, are no longer on the market, the patents and rights to manufacture the machines and suppositories having been sold to Burroughs, Wellcome & Co., of London, England.

as are shown in Figs. 323 and 324, the tubes are usually swabbed with a woollen rag carrying some liquid petrolatum or olive oil, to prevent adhesion of the material. When made with cacao butter or soap and starch they can either be compressed or formed by hand. Nasal bougies should be about 38 millimeters (1½ inches) in length and 6 millimeters (¼ inch) in diameter, while urethral bougies are

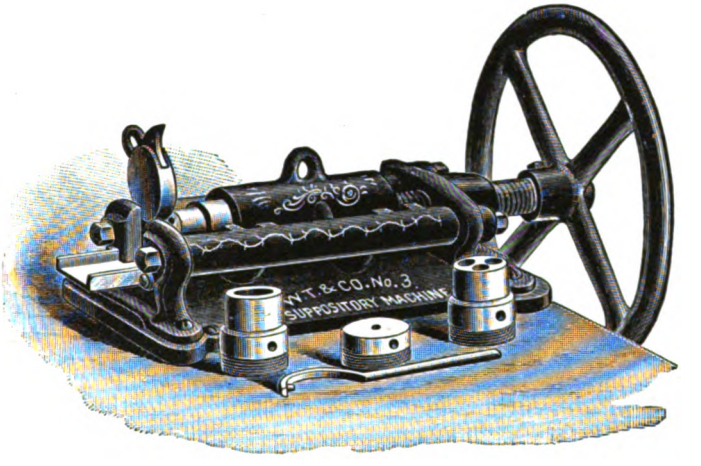


FIG. 322.—Whitall's suppository machine.

usually made 100 millimeters (4 inches) in length and from 3 to 4 millimeters (⅛ to ⅙ inch) in diameter. The ends of both are somewhat pointed, as shown in Figs. 305, 310, and 311.

The Pharmacopœia recognizes only one special kind of suppositories, viz., those of glycerin, and gives general directions for the preparation of all others. The official glycerin suppositories are composed of 93 per cent. of glycerin and 7 per cent. of sodium stearate, and if all water has been expelled, will weigh about 3.215 Gms. (50 grains) each. They are made by dissolving 0.5 Gm. of monohydrated sodium car-

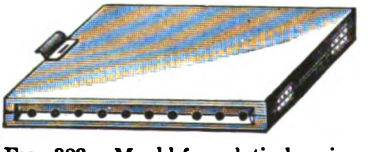


FIG. 323.—Mould for gelatin bougies.

bonate in 5 Gms. of water on a waterbath, adding first 30 Gms. of glycerin and then 2 Gms. of stearic acid, and finally heating carefully until carbon dioxide ceases to be evolved and a clear liquid results, which is then poured into a mould arranged for 10 suppositories and allowed to congeal. Since each molecule of stearic acid is capable of forming one molecule of sodium stearate, as shown by the equation

$2HC_{18}H_{35}O_2+(Na_2CO_3+H_2O)=2NaC_{18}H_{35}O_2+CO_2+2H_2O$, 2 Gms. of the acid will form 2.155+Gms. of sodium stearate, which is sufficient to form a solid mass with 30 Gms. of glycerin, the water and carbon dioxide being dissipated. Glycerin suppositories are usually made of a differ-

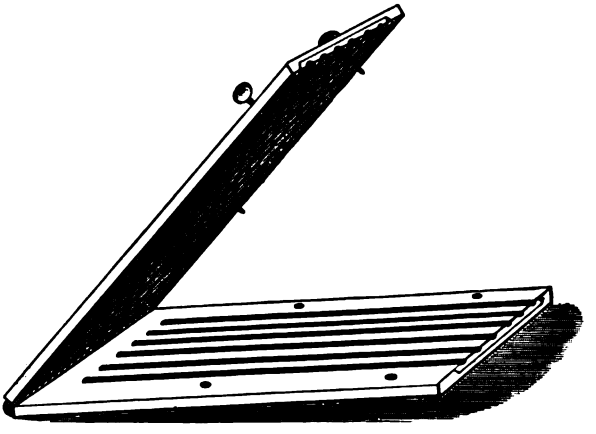


FIG. 324.—Mitchell's urethral bougie mould.

ent shape from the ordinary, being either double-pointed or having a bulbous end, as seen in Nos. 1 and 2 of Fig. 325, where also is shown a mould made by the Arthur Colton Co., of Detroit, Mich., for casting 25 double-pointed suppositories at one time. Owing to the very hygroscopic nature of glycerin, the suppositories must either be

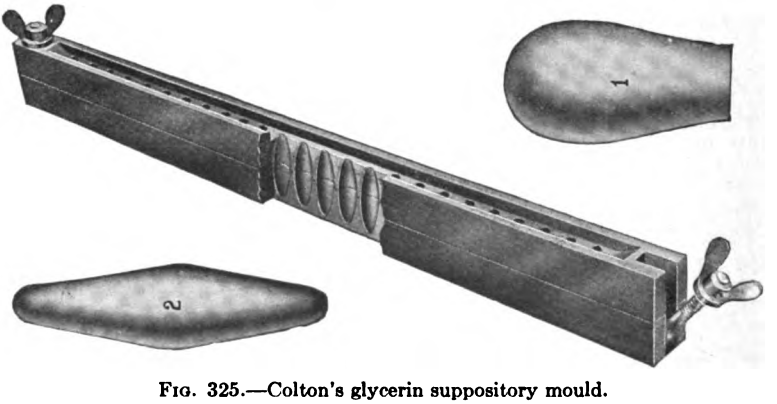


FIG. 325.—Colton's glycerin suppository mould.

wrapped in tinfoil or dispensed in small straight vials without a lip; some manufacturers coat them by dipping them into melted paraffin, which protects them against the air, but has the disadvantage of possibly failing to be removed by the patient before insertion, in which

event the suppository would fail to act, as the heat of the body is not sufficient to melt paraffin.

Suppository shells made of gelatin or butter of cacao have been introduced for the convenience of the dispenser, but are not used to

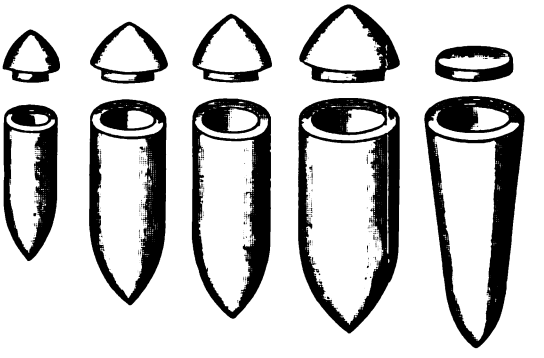


FIG. 326.—Suppository shells, made of cacao butter.

FIG. 327.—Gelatin suppository shells.

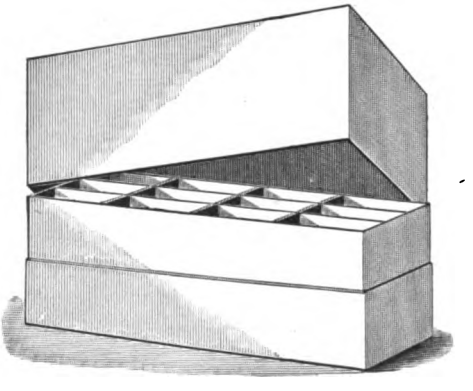


FIG. 328.—Suppository box.

any extent. The medicinal ingredient is intended to become mixed with the material of the shells as the latter melts, but, as this is uncertain, they should never be used in case of potent remedies or if the direct application of the active agent is likely to cause irritation;

for the introduction of boric acid, iodoform, or aristol they are, however, suitable. In the case of butter of cacao shells (see Fig. 326) they are preferably filled with a mixture of the active ingredient and grated butter of cacao, and the top sealed either with a warm spatula or a little stiff mucilage of acacia. The gelatin shells (see Fig. 327) may be conveniently sealed by moistening the margin of the lower half with a little water before slipping the upper part over the same. The best method of dispensing suppositories is undoubtedy in partitioned paper boxes (see Fig. 328), the sides and bottom of which should be lined with tinfoil or paraffin paper, the patient always being directed to keep the box in a cool place; in the absence of partitioned boxes, an oblong powder box may be used, the suppositories being placed between two pieces of sheet wadding.

CHAPTER XXXVI.

THE PRESCRIPTION.

ALTHOUGH the many and varied operations of the dispensing counter have been treated in the preceding chapters, a short discussion of the prescription itself seems desirable for the purpose of rendering the general information more complete.

The word *prescription* (Latin *præscriptio*, from *præ*, before and *scribere*, to write) is defined as meaning a written order or direction to the pharmacist or druggist for compounding and dispensing a medicine. A prescription consists of several parts, namely, the superscription, the inscription, the subscription, and the signature, to which is almost always added the name or initial of the physician ordering the medicine, and frequently also the name of the patient. The following prescription written out in full may serve as a type to illustrate the various parts:

(Superscription)	Recipe.
(Inscription)	Bismuthi Subnitratis, ℥j; Tincturæ Opii Camphoratæ, ℥ij; Misturæ Cretæ, q. s. ad ℥ij.
(Subscription)	Misce.
(Signature)	Signa: A teaspoonful every 2 hours.

G. W. SMITH, M. D.

For Mrs. Jenkins' infant.

The first three parts of a prescription are written, with rare exception, in the Latin language, because it is the language of science and not subject to change like modern languages. Free use is made of abbreviations, which are readily understood by pharmacists the world over. The superscription consists of a single character, R, the initial letter of the Latin word *recipe*, meaning take thou; in France the letter P is used, the initial letter of the word *prenez*. In olden times the character ♃ was usually placed at the head of prescriptions and formulas; this was the sign of Jupiter, the chief deity of the ancient Romans, and was probably intended as an invocation to the gods; a portion of this character is still used by some physicians in conjunction with the letter R, thus ℞, merely as an ornamentation and probably without any knowledge of its origin.

The inscription is the most important part of the prescription, since it contains the names and quantities of the ingredients of the medicine ordered. The names of the medicines are written in abbreviated form, and the quantities are always indicated by symbols, gr., ℈, ʒ, ℥, and Roman numerals, except in the case of metric prescriptions. In the latter case the quantities are always designated

by Arabic numerals, properly divided by the decimal point, and frequently followed by the signs Gm. or Cc.; in continental Europe the signs Gm. and Cc. are rarely employed, because Gm. is always understood, all substances, liquid as well as solid, being dispensed by weight. The inscription may be conveniently subdivided into several parts according to the importance of the several ingredients: thus, the *basis* or chief active agent; the *adjuvant* or agent second in importance, and intended to aid the basis; the *corrective*, intended to modify the action of the preceding agents; lastly, the *vehicle* or *diluent*, intended to provide a convenient and acceptable form of administration. It must not be supposed, however, that every inscription consists of four subdivisions, for sometimes only the basis and vehicle, or even the basis alone, may be prescribed.

The subscription is intended to give directions to the compounder as to the manner in which the medicine is to be dispensed, whether in divided doses or as a whole. These directions are more or less incomplete, consisting sometimes of a single letter, as *M.* for *misce*, *F.* for *fiat;* or *S.* for *solve*, or a combination of abbreviations, as *Ft. mist.* for *fiat mistura*, *Ft. pulv.* for *fiat pulvis*, *Ft. sol.* for *fiat solutio*, etc. Frequently the subscription is so incomplete as to be without meaning unless the missing portion is mentally supplied, as, for instance, *Ft. chart. x*, so often written when the physician desires the medicine to be divided into 10 powders; literally translated, this subscription would read, 10 *papers may be made* (*fiant chartæ decem*). The missing portion to be supplied may be *p. et div. in*, and if added to the above abbreviation causes the same to read, *fiat pulvis et divide in chartas x*, or *let a powder be made and divide into 10 papers*. In order to be able to read physicians' prescriptions intelligently and to write the abbreviated names and terms out in full when desired, it is necessary to be familiar with the numerous Latin titles of medicines and the many words used in the subscription. For convenience of study and reference, a table of abbreviations likely to occur in prescriptions is given on page 530.

The signature, or directions as to how the medicine is to be taken is always written in English in this country, while in Great Britain the Latin language is still occasionally used. It is important that the signature be written in a clear, legible hand, so that neither dispenser nor patient be left in doubt as to the dose intended, and it is very unfortunate that some physicians will persist in giving verbal directions to their patients and marking their prescriptions simply *use as directed*, which may lead to much confusion.

The following prescriptions are given for the purpose of acquainting the student with the use of various abbreviations common in prescription writing, and which, by a careful comparison of the abbreviated and unabbreviated forms and subsequent reference to the translation, will enable him to become familiar with this part of the work of the dispensing counter.

Abbreviated Form.	Unabbreviated Form.	Translation.
℞	Recipe	Take
Quin. Sulph. . . . . gr. xxiv.	Quininæ Sulphatis — grana viginiti quatuor.	Of Sulphate of Quinine . . 24 grains.
Ferr. Sulph. . . . . gr. vj.	Ferri Sulphatis — grana sex.	Of Sulphate of Iron . . . 6 grains.
Magn. Sulph. . . . . ʒij.	Magnesii Sulphatis — drachmas duas.	Of Sulphate of Magnesium 2 drachms.
Acid. Sulph. Ar. . . . q. s.	Acidi Sulphurici Aromatici — quantum sufficiat.	Of Aromatic Sulphuric Acid so much as may suffice.
Syr. Aurant. . . . . ℥j.	Syrupi Aurantii — unciam unam.	Of Syrup of Orange . . . . 1 ounce.
Aq. Dest. . . . . ℥v.	Aquæ Destillatæ — uncias quinque.	Of Distilled Water . . . . 5 ounces.
Ft. sol.	Fiat solutio.	Let a solution be made.
℞	Recipe	Take
Ext. Bellad. Fol. . . . gr. xxx.	Extracti Belladonnæ Foliorum — grana triginta.	Of Extract of Leaves of Belladonna . . . . . 30 grains.
Camph. Trit. . . . . ℈ij.	Camphoræ Tritæ — scrupulos duos.	Of Ground Camphor . . . 2 scruples.
P. Gallæ . . . . . ʒj.	Pulveris Gallæ — drachmam unam.	Of Powdered Nutgall . . . 1 drachm.
Adip. Benz. . . . . ℥j.	Adipis Benzoinati — unciam unam.	Of Benzoinated Lard . . . 1 ounce.
M. ft. ungt. d. ad oll.	Misce; fiat unguentum, detur ad ollam.	Mix; let an ointment be made; let it be put into a jar.
℞	Recipe	Take
Bism. Subcarb.	Bismuthi Subcarbonatis	Of Bismuth Subcarbonate
Sod. Bicarb. . . . āā ʒij.	Sodii Bicarbonatis — ana drachmas duas.	Of Sodium Bicarbonate of each 2 drachms.
Tinct. Nuc. Vom. . . . ʒj.	Tincturæ Nucis Vomicæ — drachmam unam.	Of Tincture of Nux Vomica 1 drachm.
Glycerin. . . . . ℥j.	Glycerini — unciam unam.	Of Glycerin . . . . . 1 ounce.
Aq. Menth. Pip. q. s. ad ℥iv.	Aquæ Menthæ Piperitæ — quantum sufficiat ad uncias quatuor.	Of Water of Peppermint . so much as may suffice to (make the volume) 4 ounces.
Ft. mist.	Fiat mistura.	Let a mixture be made.
℞	Recipe	Take
P. Opii . . . . . gr. v.	Pulveris Opii — grana quinque.	Of Powder of Opium . . . 5 grains.
Camph. . . . . gr. x.	Camphoræ — grana decem.	Of Camphor . . . . . 10 grains.
Sacch. Alb. . . . . gr. xv.	Sacchari Albi — grana quindecim.	Of White Sugar . . . . . 15 grains.
M. ft. p. div. in p. æq. No. x; disp. in ch. cer.	Misce; fiat pulvis; divide in partes æquales numero decem; dispensentur in charta cerata.	Mix; let a powder be made · divide into equal parts 10 in number; let them be dispensed in waxed paper.

Abbreviated Form.	Unabbreviated Form.	Translation.
℞	Recipe	Take
Hyd. Chlor. Mit. . . . gr. ij.	Hydrargyri Chloridi Mitis grana duo.	Of Mild Chloride of Mercury 2 grains.
Sacch. Alb. . . . . ʒ j.	Sacchari Albi scrupulum unum.	Of White Sugar . . . . . 1 scruple.
M. ft. p. in ch. xij div.	Misce; fiat pulvis in chartas duodecim dividendus.	Mix; let a powder be made to be divided into 12 papers.
℞	Recipe	Take
Zinc. Oxid. Opt. . . . ʒij.	Zinci Oxidi, optimi drachmas duas.	Of Oxide of Zinc, best . . . 2 drachms.
Sem. Lycopod. . . . . ℥ss.	Seminis Lycopodii unciam dimidiam.	Of Seed of Lycopodium . . ½ ounce.
Ol. Rosæ . . . . . gtt. v.	Olei Rosæ guttas quinque.	Of Oil of Rose . . . . 5 drops.
Amyl. Maid. . . q. s. ad ʒij.	Amyli Maidis quantum sufficiat ad uncias duas.	Of Corn Starch . . . . . so much as may suffice to (make the weight) two ounces.
M. ft. p. subt. d. ad scat.	Misce; fiat pulvis subtilissimus; detur ad scatulam.	Mix; let a very smooth powder be made; let it be put in a box.
℞	Recipe	Take
Ol. Tereb. . . . . ʒij.	Olei Terebinthinæ drachmas duas.	Of Oil of Turpentine . . 2 drachms.
Ol. Ricin. . . . . ʒj.	Olei Ricini unciam unam.	Of Castor Oil . . . . . 1 ounce.
P. Acac. . . . . q. s.	Pulveris Acaciæ quantum sufficiat.	Of Powder of Acacia . . . so much as may suffice.
Syr. Tolut. . . . . ℥j.	Syrupi Tolutani unciam unam.	Of Syrup of Tolu . . . . . 1 ounce.
Aq. Cinnam. . . . . ʒij.	Aquæ Cinnamomi uncias duas.	Of Water of Cinnamon . . 2 ounces.
M. ft. emuls. sec. art.	Misce; fiat emulsio secundum artem.	Mix; let an emulsion be made according to art.
℞	Recipe	Take
Pot. Brom. . . . . 15.0 Gm.	Potassii Bromidi grammata quindecim.	Of Bromide of Potassium . 15 grams.
Aq. Menth. Vir. . . . 125.0 Cc.	Aquæ Menthæ Viridis centimetra cubica centum et viginti quinque.	Of Water of Spearmint . . 125 cubic centimeters.
Ft. sol.	Fiat solutio.	Let a solution be made.
℞	Recipe	Take
Plumb. Acet. . . . . 1.5 Gm.	Plumbi Acetatis gramma unum et dimidium.	Of Acetate of Lead . . . . 1½ grams.
P. Opii . . . . . 0.65 "	Pulveris Opii centigrammata sexaginta quinque.	Of Powder of Opium . . . 65 centigrams.
Camph. . . . . 0.50 "	Camphoræ decigrammata quinque.	Of Camphor . . . . . 5 decigrams.
M. ft. mass. in pil. xij div.	Misce; fiat massa in pilulas duodecim dividenda.	Mix; let a mass be made to be divided into 12 pills.

Abbreviated Form.	Unabbreviated Form.	Translation.
℞	Recipe	Take
Cocain. Hydrochl. . 0.20 Gm.	Cocainæ Hydrochloridi decigrammata duo.	Of Hydrochloride of Cocaine 2 decigrams.
Ac. Borac. . . . . 0.32 "	Acidi Boracici centigrammata triginta duo.	Of Boracic Acid . . . . . 32 centigrams.
Aq. Dest. . . . . 10.0 Cc.	Aquæ Destillatæ centimetra cubica decem.	Of Distilled Water . . . . 10 cubic centimeters.
M. ft. collyr. filt.	Misce, fiat collyrium: filtra.	Mix; let an eyewash be made; filter.
℞	Recipe	Take
Ferr. Sulph. Cryst. . 6.0 Gm.	Ferri Sulphatis Crystallisati grammata sex.	Of Crystallized Sulphate of Iron . . . . . 6 grams.
Myrrh. Elect.	Myrrhæ electæ	Of Select Myrrh .
Sacch. Alb. . . āā 18.0 Gm.	Sacchari Albi ana grammata octodecim	Of White Sugar . of each 18 grams.
Pot. Carb. . . . . 8.0 "	Potassii Carbonatis grammata octo.	Of Carbonate of Potassium . 8 grams.
Spir. Lavand. . . . 60.0 Cc.	Spiriti Lavandulæ centimetra cubica sexaginta.	Of Spirit of Lavender . . . 60 cubic centimeters.
Aq. Rosæ . q. s. ad 1000.0 "	Aquæ Rosæ quantum sufficiat ad centimetra cubica mille.	Of Rose water . . . so much as may suffice to (make the volume) 1000 cubic centimeters.
Ft. mist.	Fiat mistura.	Let a mixture be made.
℞	Recipe	Take
Acid. Arsen. . . . . 0.002 Gm.	Acidi Arsenosi milligrammata duo.	Of Arsenous Acid . . . . 2 milligrams.
P. Piper. Nig. . . . 0.065 "	Pulveris Piperis Nigri milligrammata sexaginta quinque.	Of Powder of Black Pepper 65 milligrams.
M. ft. pil. d. tal. dos. No. xxx.	Misce; fiat pilula; dentur tales doses numero triginta.	Mix; let a pill be made; let such doses be given 30 in number (let 30 such doses be given).
℞	Recipe	Take
Sod. Carb. . . . . 3.0 Gm.	Sodii Carbonatis grammata tria.	Of Carbonate of Sodium . . 3 grams.
Acid. Stearic. . . . . 5.0 "	Acidi Stearici grammata quinque.	Of Stearic Acid . . . . . 5 grams.
Glycerin. . . . . 60.0 "	Glycerini grammata sexaginta.	Of Glycerin . . . . . 60 grams.
M. ft. mass. ex qua form. suppos. rect. No. x; dent. ad vitr. ben. claus.	Misce; fiat massa ex quâ formentur suppositoria rectalia numero decem; dentur ad vitrum bene clausum.	Mix; let a mass be made out of which may be formed rectal suppositories 10 in number; let them be put into a well-closed bottle.
℞	Recipe	Take
Sod. Salicyl. . . . . 15.0 Gm.	Sodii Salicylatis grammata quindecim.	Of Salicylate of Sodium . . 15 grams.
D. in p. æq. No. xij; d. ad caps. amyl.	Divide in partes æquales numero duodecim; dentur ad capsulas amylaceas.	Divide into equal parts, 12 in number; let them be put into starch capsules (wafers or cachets).

It will be observed in the above prescriptions that in every instance the ingredients are written in the genitive (possessive) case, and the quantities, whether by weight or measure, in the accusative (objective) case. This arrangement will be better understood after the analysis of the following prescription has been carefully studied.[1]

℞—Potassii Citratis . . . . . ℥ij (drachmas duas).
Spiritus Ætheris Nitrosi . . } āā ℥ij (ana drachmas duas).
Vini Colchici Radicis . . . }
Syrupi Acidi Citrici . . . . ℥j (unciam unam).
Aquæ Menthæ Viridis . . q. s. ad ℥iv (quantum sufficiat ad uncias quatuor).
Ft. sol. (fiat solutio).

As explained on page 523, the letter *R* stands for the word *Recipe*, the imperative mood of the transitive verb *Recipio, recipere, recepi, receptum*, third conjugation, meaning to receive or to take; hence the imperative *Recipe* means "take thou," and the object of the verb, in this case the quantity of ingredient ordered, must be in the accusative (objective) case, according to the rule, that a transitive verb in the active voice governs a noun in the objective case. The word *recipe* although indicated but once, at the head of the prescription, must be understood as governing the quantity of every ingredient prescribed.

Potassii (of potassium) is the genitive singular of *potassium*, a neuter noun of the second declension, and is governed by *citratis*, according to the rule that a noun limiting the signification of another noun governs the same in the genitive (possessive) case.

Citratis (of citrate) is the genitive singular of *citras*, a masculine noun of the third declension, and is governed by *drachmas*, according to the rule that a noun denoting quantity, quality, or property governs another noun, to which it is so related, in the genitive case.

Drachmas (drachms) is the accusative plural of *drachma*, a feminine noun of the first declension, and is the object of the verb *recipe*.

Duas (two) is the accusative plural feminine of the numeral adjective *duo, duæ, duo*, and qualifies *drachmas*, with which it must agree in case, number, and gender.

Spiritus (of spirit) is the genitive singular of *spiritus*, a masculine noun of the fourth declension, and is governed by *drachmas*, according to the rule stated under *citratis*.

Ætheris (of ether) is the genitive singular of *æther*, a masculine noun of the third declension, and is governed by *spiritus*, according to the rule given under *potassii*.

Nitrosi (of nitrous) is the genitive singular masculine of the adjective *nitrosus, nitrosa, nitrosum*, and qualifies *ætheris*, according to the rule given under *duas*.

[1] Students desirous of gaining further information on this subject are referred to the following books: Robinson's *Latin Grammar of Pharmacy and Medicine; The Latin Grammar of Pharmacy*, by Joseph Ince (England), and *Elements of Latin for Students of Pharmacy and Medicine*, by Crothers and Bice.

Vini (of wine) is the genitive singular of *vinum*, a neuter noun of the second declension, and is governed by *drachmas*, according to the rule given under *citratis*.

Colchici (of colchicum) is the genitive singular of *colchicum*, a neuter noun of the second declension, and is governed by *radicis*, according to the rule given under *potassii*.

Radicis (of root) is the genitive singular of *radix*, a feminine noun of the third declension, and is governed by *vini*, according to the rule given under *potassii*.

Ana (of each) is a Greek preposition governing the accusative case, and as such has a distributive effect. Although the abbreviated form āā is extensively employed, it would seem more correct to use instead the Latin adjective *singulorum* to indicate "of each," usually abbreviated *sing.*, and this is done by some physicians, particularly in Germany. The abbreviation āā or *sing.* may be used in connection with any number of ingredients and is usually written opposite the last one of the series to which it is intended to apply.

Drachmas (drachms) as above.

Duas (two) as above.

Syrupi (of syrup) is the genitive singular of *syrupus*, a masculine noun of the second declension, and is governed by *unciam*, according to the rule given under *citratis*.

Acidi (of acid) is the genitive singular of *acidum*, a neuter noun of the second declension, and is governed by *syrupi*, according to the rule given under *potassii*.

Citrici (of citric) is the genitive singular neuter of the adjective *citricus, citrica, citricum*, and qualifies *acidi*, according to the rule given under *duas*.

Unciam (ounce) is the accusative singular of *uncia*, a feminine noun of the first declension, and is the object of the verb *recipe*.

Unam (one) is the accusative singular feminine of the numeral adjective *unus, una, unum*, and qualifies *unciam*, according to the rule given under *duas*.

Aquæ (of water) is the genitive singular of *aqua*, a feminine noun of the first declension, and is governed by *tantum*, understood (see *quantum*), according to the rule given under *citratis*.

Menthæ (of mint) is the genitive singular of *mentha*, a feminine noun of the first declension, and is governed by *aquæ*, according to the rule given under *potassii*.

Viridis (of green) is the genitive singular feminine of the adjective *viridis, viridis, viride*, and qualifies *menthæ*, according to the rule given under *duas*.

Quantum (how much) may be parsed as an adverb of quantity qualifying the verb *sufficiat*, but it is better to parse it as a relative adjective with the adjective *tantum* (so much) as its redditive. In either case the adjective *tantum* is understood and governs *aquæ*,

according to the rule that adjectives in the neuter gender, without a substantive, are regarded as nouns and govern the genitive case. *Tantum* is never used jointly with *quantum* in prescriptions, but the former is always understood, and the translation, whether both words are used or only the latter, is invariably "so much as."

Sufficiat (may suffice or may be sufficient), is the third person singular, subjunctive mood, present tense, of the intransitive verb *sufficio, sufficere, suffeci, suffectum*, third conjugation, meaning to suffice or to be sufficient, and is governed by *quantum* as its subject.

Ad (to) is a preposition governing the accusative *uncias*.

Uncias (ounces) is the accusative plural of *uncia*, a feminine noun of the first declension, and is governed by the preposition *ad*.

Quatuor (four) is an indeclinable numeral adjective and qualifies *uncias*.

Fiat (may be made or let there be made) is the third person singular, subjunctive mood, present tense, of the irregular verb *fio, fieri, factus*, meaning to be made or done, and has *solutio* for its subject.

Solutio (solution) is the nominative singular of *solutio*, a feminine noun of the third declension, and is the subject of the verb *fiat*.

LIST OF ABBREVIATIONS AND TERMS USED IN PRESCRIPTIONS.

Abbreviation.	Term or Phrase.	Meaning.
ā or āā	ana	of each.
Add. or Addat.	Adde or addatur	Add or let it be added.
Ad. libit.	Ad libitum	At pleasure.
Aeq.	Aequalis, is, e	Equal.
Agit. or Agitet.	Agita or agitetur	Shake or let it be shaken.
Alb.	Albus, a, um	White.
Ant.	Ante	Before.
Arom.	Aromaticus, a, um	Aromatic.
Aq.	Aqua	Water.
Aq. bull.	Aqua bulliens	Boiling water.
Aq. ferv.	Aqua fervida	Hot water.
Aq. saturn.	Aqua saturni	Lead water.
Aq. phaged. fl.	Aqua phagedenica flava	Yellow wash.
Aq. phaged. nig.	Aqua phagedenica nigra	Black wash.
Aquil. alb.	Aquila alba	Calomel.
Argill.	Argilla	Clay.
Bacill.	Bacillum	Bougie.
Baln. aren.	Balneum arenæ	Sand bath.
Baln. mar.	Balneum maris	Saltwater bath.
Baln. vap.	Balneum vaporis	Steam bath.
Ben.	Bene	Well.
B. or Bis. i. d.	Bis in die	Twice a day.
Brev.	Brevis, is, e	Short.
Bull.	Bulliat or bulliant	Let it (or them) boil.
Cærul.	Cæruleus, a, um	Blue.
Calef.	Calefactus, a, um	Warmed.
Cap.	Capiat	May be taken.
Caps.	Capsula	Capsule.
Caps. amyl.	Capsulæ amylaceæ	Cachets.
Caps. gelat.	Capsulæ gelatinosæ	Gelatin capsules.
Carbas.	Carbasus	Lint.

Abbreviation.	Term or Phrase.	Meaning.
Cœn.	Cœna or cena.	Supper.
Cer. or Cerat.	Ceratum or Ceratus, a, um	Cerate Waxed.
Chart.	Charta	Paper.
Chartul.	Chartula	Small paper.
Ch. cer. or Chart. cerat.	Charta cerata	Waxed paper.
Chart. pergam.	Charta pergamentoria	Parchment paper.
Cib.	Cibus	Food.
Cito disp.	Cito dispensetur.	Let it be dispensed quickly.
Claus.	Clausus, a, um	Closed, inclosed.
Cochl.	Cochlear	Spoon.
Cochl. magn.	Cochlear magnum	A large (table) spoon.
Cochl. parv.	Cochlear parvum	A small (tea) spoon.
Cochl. mod.	Cochlear modicum	A medium (dessert) spoon.
Col. or Colet.	Cola or coletur	Strain or let it be strained.
Collun.	Collunarium	A nose wash.
Collut.	Collutorium	A mouth wash.
Collyr.	Collyrium	An eye wash.
Consp.	Conspergе	Dust or sprinkle.
Contus.	Contunde or contusus	Bruise or bruised.
Coq.	Coque	Boil.
Cong.	Congius	Gallon.
Comp.	Compositus, a, um	Compound.
D.	Da, detur, or dentur	Give, it (or they) may be given.
D. or dent. t. d.	Da or dentur tales doses	Give or let there be given such doses.
Det. or dent.	Detur or dentur	Let there be given.
Dec. or decoct.	Decoctum	Decoction.
De d. in d.	De die in diem	From day to day.
Dieb. alt.	Diebus alternis	Every other day.
Dig.	Digere or digeretur	Digest or it may be digested.
Disp.	Dispensetur or dispensentur	Let there be dispensed.
Div. or divid.	Divide, dividatur or Dividendus, a, um	Divide or it may be divided. To be divided.
Dos.	Dosis or doses	Dose or doses.
Elect.	Electuarium	Electuary.
Emp. or Empl.	Emplastrum	Plaster.
Empl. lytt.	Emplastrum lyttæ	Blistering plaster.
Empl. epist.	Emplastrum epispasticum	Blistering plaster.
Empl. vesic.	Emplastrum vesicans or vesicatorium	Blistering plaster.
Emuls.	Emulsio	Emulsion.
Emuls. oleos.	Emulsio oleosa	Oil emulsion.
Epist. or Epistom.	Epistomium	Stopper.
Epist. elast.	Epistomium elasticum	Rubber stopper.
Epist. vitr.	Epistomium vitreum	Glass stopper.
E. m. p.	Ex modo præscripto	As directed.
Ex aq.	Ex aqua	From (with) water.
Ex qua form.	Ex qua formentur	From which there may be formed.
Extend.	Extende	Spread.
Ext. sup. cor.	Extende supra corium	Spread upon leather.
Ext. sup. alut.	Extende supra alutam	Spread upon leather.
Ext. or Extr.	Extractum	Extract.
Ext. or Extr. fl.	Extractum fluidum	Fluid extract.
F. or Ft.	Fiat or fiant	Let there be made.
F. l. a.	Fiat lege artis	Let there be made according to (by the law of) art.
F. s. a.	Fiat secundum artem	Let there be made according to art.
Ferv.	Fervidus, a, um,	Hot.

Abbreviation.	Term or Phrase.	Meaning.
Filt.	Filtra	Filter.
Flav.	Flavus, a, um	Yellow.
Fld.	Fluidus, a, um	Fluid.
Frig.	Frigidus, a, um	Cold.
Garg.	Gargarisma	Gargle.
Gm.	Gramma or grammata	Gramme or grammes.
Gtt. or Gutt.	Gutta or guttæ	Drop or drops.
Gr.	Granum or grana	Grain or grains.
Guttat.	Guttatim	By drops.
Haust.	Haustus	Draught.
Hor. somn.	Hora somnis	At bed-time.
Inf.	Infunde or infusum	Infuse or infusion.
L. a.	Lege artis	According to (by the law of) art.
Lin. or Linim.	Linimentum	Liniment.
Liq.	Liquor	Liquor or solution.
Mac. or Macer.	Macera	Macerate.
Levit.	Leviter	Lightly.
Levit. claus.	Leviter clausus, a, um	Lightly or loosely closed.
Lut.	Luteus, a, um	Golden yellow.
Mag.	Magnus, a, um	Large.
Mass.	Massa	Mass.
M. or Misc.	Misce or misceantur	Mix or let them be mixed.
M. bene	Misce bene	Mix well.
M. caute	Misce caute	Mix cautiously.
Mist.	Mistura	Mixture.
Mod.	Modicus, a, um	Moderate (sized).
Mic. pan.	Mica panis	Crumb of bread.
Mit.	Mitte or mittatur	Send or let there be sent.
Mit. tal.	Mitte or mittantur tales	Send or let there be sent such.
Nig.	Niger, nigra, nigrum	Black.
No.	Numero	By or in number.
Non-rep.	Non-repetatur	It is not to be repeated.
O.	Octarius	Pint.
Obduc.	Obduce or obducatur	Cover or let it be covered.
Obduct.	Obductus, a, um	Covered, coated.
Ol.	Oleum	Oil.
Oleos.	Oleosus, a, um	Oily, made of oil.
Oll.	Olla	Jar.
Omn. hor.	Omni hora	Every hour.
Omn. man.	Omni mane	Every morning.
Omn. noct.	Omni nocte	Every night.
Opt.	Optimus, a, um	Best.
P. or Part.	Pars or partes	Part or parts.
P. or Part. æq.	Partes æquales	Equal parts.
P. c., p. cib., or post cib.	Post cibum	After food.
P. r. n.	Pro re nata	As occasion arises; as needed; occasionally.
P. or post prand.	Post prandium	After dinner.
P. or Pulv.	Pulvis or pulveres	Powder or powders.
Par.	Para, paretur, or paratus	Prepare, let it be prepared, or prepared.
Parv.	Parvus, a, um	Small.
Pil. or Pilul.	Pilula or pilulæ	Pill or pills.
Pulv. gross.	Pulvis grossus	Coarse powder.
Pulv. subt.	Pulvis subtilissimus	Very smooth powder.
Q. l. or Q. p.	Quantum libet or Quantum placet	As much as you please.
Q. s.	Quantum satis, Quantum sufficit, or Quantum sufficiat	A sufficient quantity.

Abbreviation.	Term or Phrase.	Meaning.
R. or Recip.	Recipe	Take thou.
Rept.	Repetatur	Let it be repeated.
Rub.	Ruber, rubra, rubrum	Red.
S. a.	Secundem artem	According to art.
S. l.	Secundem legem	According to law.
S. or Solv.	Solve or solvatur	Dissolve or let it be dissolved.
Scat.	Scatula	Box.
Sem.	Semen or semina	Seed.
Sig.	Signa or signetur	Mark (label) or let it be marked (labeled).
Simp.	Simplex	Simple.
Sing.	Singulorum	Of each.
Sol. or Solut.	Solutio	Solution.
Spiss.	Spissus, a, um	Hard.
Supp. or Suppos.	Suppositorium or suppositoria	Suppository or suppositories.
Sum.	Sume or sumatur	Take or let there be taken.
Syr. or Syrup.	Syrupus	Syrup.
Tab.	Tabella or tabellæ	Tablet or tablets.
Tal.	Talis or tales	Such.
T. or ter i. d.	Ter in die	Three times a day.
Ter.	Tere	Rub or triturate.
Tinct. or. Tr.	Tinctura	Tincture.
Troch.	Trochiscus or trochisci	Lozenge or lozenges.
Ungt.	Unguentum	Ointment.
Ust.	Ustus, a, um	Burned.
Ut dict.	Ut dictum	As directed.
Vitr.	Vitreus, a, um, or vitrum	Of glass or glass.

In addition to the date usually marked on the prescription, it is customary also to place a number thereon, for the purpose of ready reference in case the prescription is to be repeated. Such numbering may be done with pen and ink, but it is preferably imprinted with a numbering machine, since the latter has the great advantage of obviating the danger of duplication of the same number on two or more prescriptions. In Fig. 329 is shown such an automatic numbering machine, which can be arranged so as to print numbers in duplicate or triplicate if desired and then changes automatically after producing each set; it can be made to print consecutive numbers, or repeat the same number indefinitely. The figures from which the machine prints are made of steel, and are freshly inked after each movement of the machine; all parts are interchangeable. The numbering capacity ranges from 1-9999 to 1-9999999, according to the number of wheels with which the machine is supplied.

For the preservation of prescriptions various devices are in use. Some pharmacists simply file the prescriptions on a heavy steel wire, claiming that, as the repetitions are few in number comparatively, this plan is convenient and less laborious than others. In some stores the prescriptions are pasted into large scrap books, especially made for that purpose, the leaves of which are of heavy manilla paper and secured to a wood back, the binding being of stout canvas. In Fig. 330 may be seen one of the styles of prescription books which serves the purpose admirably of preserving the original prescriptions intact.

Some pharmacists prefer to put the prescriptions up carefully in bundles of one hundred or more, between thin boards, and storing them in boxes in drawers of a cabinet, appropriately marked. Lastly, a few still follow the plan, at one time much in vogue, of copying the prescriptions into a book kept for that purpose; this plan, while no doubt convenient for reference, is open to the serious objection of possible errors made in copying, and must therefore be carried out with great care.

The ownership of the prescription is still an unsettled question. While some claim that the prescription is simply an order on the pharmacist from the physician, and that therefore the former is the proper custodian of the same, there are others who insist that the

FIG. 329.—Bates' automatic numbering machine.

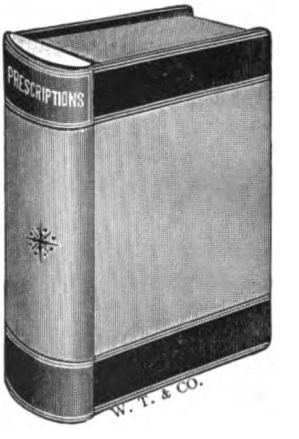


FIG. 330.—Whitall's prescription book.

prescription is but the written advice of the physician to his patient, for which the latter has paid, and to the sole ownership of which he has full legal right, as much so as a client has to the written opinion of his lawyer whom he has consulted and paid. The latter view prevails in Germany, where prescriptions are never retained by the pharmacist, but invariably handed back to the customer with the medicine, except in cases where the medicine is not paid for at the time of delivery, the prescription being held until payment is made and then returned. As a rule, the original prescription is retained by the pharmacist in this country, who, however, rarely refuses to give a copy to the customer if the same is asked for; this plan seems most desirable, as it leaves in the hands of the pharmacist the only

legal evidence of what the physician has actually prescribed, in case a dispute should arise as to the correct dispensing of the medicine.

The indiscriminate repetition of medicine, especially if the latter be of a potent or dangerous character, is to be strongly condemned. Serious results have been known to follow the unwarranted repeated dispensing of medicines containing cocaine hydrochloride, morphine sulphate, and similar dangerous preparations. Fortunately this custom has been broken up by the Harrison Act passed by Congress in 1914, which forbids the refilling of prescriptions containing cocaine and morphine and their salts and derivatives. Some physicians severely criticise the repetition of any prescription without special order, but forget that the pharmacist may have no knowledge of the

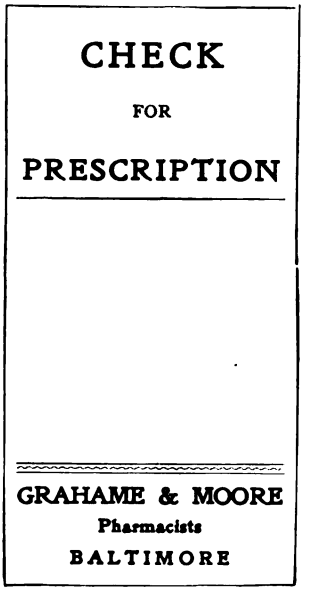


FIG. 331.

physician's wishes in this respect, since a verbal order to have the medicine refilled is frequently given to the patient by the physician. The words "Not to be repeated," placed at the head of the prescription would prove an easy and effectual means of preventing repetition without the physician's order, for every respectable pharmacist would promptly and cheerfully comply with such a request. In the absence of instructions from the physician, the request for a copy of a prescription by the customer, or for repetition of any ordinary medicine, cannot well be refused, but judgment is necessary in order that the original prescription be not abused and made to do service for a number of outside persons who have no claim upon it, whereby the physician would be made to suffer financially.

In order to guard against confusion and mistakes in the compounding and delivery of medicines, a check system is in use in many stores, and is to be highly commended. The best of these is probably the following: When a prescription is handed in by a customer, it is at once numbered by the person receiving it and at the same time two checks, made of pasteboard and of the size and style shown in Fig. 331, are stamped with the same number by means of the automatic numbering machine mentioned above. One of the checks is handed to the customer and the other accompanies the prescription to the dispensing counter, to be afterward attached to the bottle, box, or jar of medicine when completed. On this second check are also marked the price of the medicine, whether paid or not, and such other information as may appear desirable.

For further detailed information regarding the numerous and often perplexing operations of the dispensing counter, the reader is referred to two excellent books, containing much valuable information, namely, *The Art of Compounding*, by Prof. W. L. Scoville, of Detroit, Mich., and *The Art of Dispensing*, by P. MacEwan, Esq., of London, England.

PART III.

PHARMACEUTICAL CHEMISTRY.

ALTHOUGH the term *pharmaceutical chemistry* is objected to by many who rightfully claim that there can be but one kind of chemistry, the laws and principles of which must be the same whether applied to pharmacy, medicine, physiology, or agriculture, it will, nevertheless, be retained in this book as a convenient heading under which to group the many details of composition, preparation, and examination of that vast number of chemical compounds in almost daily use by pharmacists, and the majority of which are officially recognized in the U. S. Pharmacopœia. The classification of chemical compounds with regard to constitution, etc., will, in the main, not be based upon the views at present accepted by chemists, concerning which the student of pharmacy receives ample instruction in his chemical lectures, and of which he can find full explanation in the many excellent chemical text-books of today; but a somewhat unsystematic arrangement will be followed, having in view more particularly the study of official and other chemicals from a pharmaceutical standpoint irrespective of their chemical relationship. After an experience of many years this plan, being still found the most desirable for pharmacists, is adhered to in pharmaceutical schools.

Chemical compounds may be conveniently divided into those usually designated as inorganic substances and those formerly known as organic compounds, but to which now the name carbon compounds is more appropriately applied.

INORGANIC SUBSTANCES.

Of the 15 elements which are known as non-metallic bodies, all but 5 are of pharmaceutical interest, either because they are employed extensively by physicians in their elementary state or because they form certain important compounds with each other which are officially recognized in the Pharmacopœia; such compounds only will be considered here, and these are furnished by the following elements: hydrogen, oxygen, nitrogen, chlorine, bromine, iodine, sulphur, phosphorus, carbon, and boron. A very valuable class of compounds formed by these elements are the inorganic acids, which will be treated in a separate chapter.

Combinations of non-metallic elements with the metals are very properly classified as compounds of the latter, and will be considered in connection with the salts and numerous other preparations of the metals, officially recognized. The compounds of metals may be conveniently considered according to a system which groups those metals together the oxides of which possess certain well recognized properties in common; thus, metals of the alkalies, of the alkaline earths, of the earths and heavy metals.

Since very few metallic salts are prepared by pharmacists, such compounds will be treated chiefly with a view of enabling the student to understand fully the official requirements as regards identity and quality, detailed consideration being given mainly to those compounds for the preparation of which the Pharmacopœia gives official working formulas.

CHAPTER XXXVII.

HYDROGEN, NITROGEN, AND OXYGEN.

NEITHER hydrogen nor nitrogen is of pharmaceutical value in its uncombined gaseous state, but they unite with oxygen to form some very important compounds.

The most important compound of hydrogen and oxygen is water, which may be looked upon chemically as hydrogen monoxide, H_2O. The Pharmacopœia recognizes both natural and distilled water, and while in some localities natural water may be obtained remarkably free from impurities, the use of distilled water is to be preferred at the dispensing counter and for the preparation of aromatic waters and many chemical solutions. While the official limit for the presence of inorganic impurities, as shown by the residue upon evaporation of the water, is fixed at $\frac{3}{1000}$ per cent. (0.3 Gm. in 1000 mils. or Cc.) for natural water, it has been reduced to $\frac{1}{1000}$ per cent. (0.10 Gm. in 1000 mils. or Cc.) for distilled water. Moreover, the Pharmacopœia requires that natural water mixed with 10 per cent. of its volume of diluted sulphuric acid and 0.4 per cent. of tenth-normal potassium permanganate solution shall not become completely decolorized by boiling it for 10 minutes, showing the limit of oxygen consuming capacity as a measure of organic impurities; in the case of distilled water the limit of organic or other oxidizable substances is determined by adding only one-fourth as much of the potassium permanganate solution, as in the case of natural water, when the mixture after having been boiled for 10 minutes, should not completely lose its pink color.

Hydrogen Dioxide.—Hydrogen dioxide, H_2O_2, first obtained in 1818 by Thenard, contains 94 per cent. of oxygen, and is the richest oxygen compound known. It is officially recognized, in the form of a 3 per cent. aqueous solution, under the Latin title *Liquor Hydrogenii Dioxidi.*

The compound H_2O_2 may be obtained from any metallic dioxide which yields a portion of its oxygen to water upon treatment with an acid. For technical purposes, sodium dioxide is extensively employed, but this method is not suitable for medicinal purposes, as the resulting solution cannot be freed from the accompanying sodium sulphate or chloride. The Pharmacopœia no longer gives directions for making solution of hydrogen dioxide. That intended for medicinal use is usually made from barium dioxide, which upon saturation with an acid readily gives up one-half of its oxygen to water to form

hydrogen dioxide, as shown by the following equation: $6BaO_2 + 6H_2O + 4H_3PO_4 = 6H_2O_2 + 2Ba_3(PO_4)_2 + 6H_2O$.

An important step in the manufacture of solution of hydrogen dioxide is the thorough hydration of the barium dioxide, in order to insure rapid and complete saturation subsequently with the acid; experience has shown that cold favors hydration of the finely powdered barium dioxide, which is known to be completed when the water separates but slightly from the resulting magma. Phosphoric acid has been found to produce a larger yield of H_2O_2 than sulphuric or carbonic acid, and is even preferable to hydrochloric acid, owing to the difficulty of removing the free acid after decomposition of the barium chloride formed. Hydrofluoric acid has also been successfully employed for the liberation of hydrogen dioxide, but its corrosive nature presents great obstacles to its use, although the resulting barium fluoride is even more insoluble than the phosphate. The hydrated barium dioxide must be fully decomposed and saturated with acid to exact neutrality; about 96 mils. (or Cc.) of phosphoric acid diluted with 320 mils. (or Cc.) of distilled water will be required for 300 Gms. of barium dioxide hydrated by addition to 500 mils. (or Cc.) of cold distilled water. A portion (about 50 mils. or Cc.) of the diluted acid is set aside as a reserve, and used in small quantities after all the barium dioxide mixture has been added to the remainder of the acid, until a perfectly neutral reaction is obtained. Vigorous agitation and refrigeration of the acid and barium mixture are necessary to insure a full yield of H_2O_2. After filtration of the mixture for the purpose of removing the newly formed barium phosphate, an addition of small quantities of diluted sulphuric acid is made to the filtrate for the purpose of freeing it entirely from barium, a small portion of which will have entered into solution as acid barium phosphate; the newly formed precipitate of barium sulphate may be removed by filtration after addition of a little starch. The finished product contains a small amount of phosphoric acid, liberated from the acid phosphate, and a trace of sulphuric acid.

Solution of hydrogen dioxide readily undergoes spontaneous decomposition, particularly if exposed to heat and sunlight; it should, therefore, be preserved in a cool, dark place, in amber-colored bottles which have been not too tightly stoppered to avoid explosion in case of defective bottles and increased pressure caused by accumulation of gas. Various preservatives have been suggested to protect the solution against deterioration, among which acetanilid, in the proportion of 3 grains to a pint of the solution, has been found serviceable and is used by some manufacturers. Moderate heat is far less injurious than sunlight, and it has been found that if a temperature of 60° C. (140° F.) be not exceeded, a 50 volume solution can be readily obtained by simple concentration on a waterbath without appreciable loss of hydrogen dioxide; above this temperature, however, decomposition rapidly increases.

The Pharmacopœia demands the absence of hydrofluoric and oxalic acids, and also of barium, and limits the presence of non-volatile matter to 0.150 Gm. in 100 mils. (or Cc.) of the solution. The amount of preservative present is directed to be determined by shaking out 100 mils. (or Cc.) of solution of hydrogen dioxide with 3 successive portions (50, 25 and 25 mils. or Cc.) of a mixture of chloroform 3 volumes and ether 2 volumes, when, upon evaporation of the mixed chloroform-ether solutions, at room temperature, not more than 0.04 Gm. of residue should be left.

The strength of solution of hydrogen dioxide officially required is not less than 3 per cent. by weight of pure H_2O_2, which corresponds to about 10 volumes of available oxygen. The assay is made by diluting 2 Gms. of the solution, accurately weighed, with 20 mils. (or Cc.) of distilled water, adding 20 mils. of diluted sulphuric acid, and titrating with tenth-normal potassium permanganate solution. The following reaction ensues: $5H_2O_2 + 3H_2SO_4 + 2KMnO_4 = K_2SO_4 + 2MnSO_4 + 8H_2O + 5O_2$. Only one-half of the oxygen indicated in the equation is derived from the hydrogen dioxide, the other half being furnished by the potassium permanganate, which fact must be considered if the gas is collected and measured in a gas tube over mercury. The term available oxygen refers, therefore, to the volume of nascent oxygen obtained directly from the dioxide, and not to the total volume liberated in the reaction. From the above equation it is seen that 2 molecules (316.06 parts) of potassium permanganate correspond to 5 molecules (170.08 parts) of hydrogen dioxide; hence each mil. (or Cc.) of a tenth-normal solution of the former containing 0.0031606 Gm. of $KMnO_4$ must be equivalent to 0.0017008 Gm. of H_2O_2, or 0.0008 Gm. of oxygen available therefrom.

The volume strength of any solution of hydrogen dioxide, that is the volumes of available oxygen, can be determined either gasometrically or by titration. As stated above, only one-half of the oxygen obtained in the gasometric assay comes from the hydrogen dioxide present, and the total volume must therefore be divided by 2 and then by the number of mils. (or Cc.) of the solution taken for the assay, to obtain the exact volumes of available oxygen. As this method is out of the reach of the average pharmacist, titration with potassium permanganate is to be preferred and will give results sufficiently accurate for all practical purposes. One mil. (or Cc.) of oxygen at 0° C. and 760 mm. weighs 0.0014303 Gm. and since 1 mil. (or Cc.) of tenth-normal potassium permanganate solution corresponds to 0.0008 Gm., as shown above, the volume of oxygen corresponding to 1 mil. (or Cc.) of the potassium permanganate solution is easily ascertained by dividing 0.0014303 into 0.0008, which gives 0.559 + or practically 0.56 mil. (or Cc.). Now to find the volumes o available oxygen in any sample of hydrogen dioxide solution, 1 mil. (or Cc.) of the solution, properly acidulated with diluted sulphuric acid, should be titrated with tenth-normal potassium permanganate solu-

tion; the number of mils. (or Cc.) of the latter solution required, when multiplied by 0.56 will express the volumes of oxygen obtainable from the sample used in the test.

The reaction with potassium chromate and ether mentioned in the Pharmacopœia depends upon the formation of a new compound which forms a blue solution with ether; it is characteristic of hydrogen dioxide. By some the compound formed is considered to be perchromic anhydride (Cr_2O_7), a substance analogous to permanganic anhydride (Mn_2O_7), while others assume that it may possibly be a compound of CrO_3 and H_2O_2.

An aqueous solution of hydrogen dioxide much stronger than the one recognized in the Pharmacopœia is now on the market and sold as Perhydrol. It contains 30 per cent. of hydrogen dioxide, corresponding to about 100 volumes of available oxygen, and is miscible in all proportions with water or alcohol. Perhydrol has a specific gravity of 1.115 at 15° C. (59° F.), and must be kept in a cool place.

Oxygen.—Oxygen is the only element in gaseous form recognized in the Pharmacopœia. While it can be readily obtained by heating red oxide of mercury or a mixture of potassium chlorate and manganese dioxide in suitable retorts, it is produced on a large scale for commercial purposes by other more profitable methods. The most economical process perhaps is that in which air is first liquefied in a suitable apparatus and then fractionated or rectified in a column consisting of perforated copper plates, where mainly the nitrogen is allowed to escape, while the liquid oxygen is retained and after gradual conversion into gas, is collected in a gasometer.

Another method yielding good results is to heat sodium manganate in narrow vertical retorts to a temperature of 500° C. (932° F.) and to treat with alternate injections of steam and dry purified air, two reactions taking place, thus: $Na_2MnO_4 + H_2O = O + 2NaOH + MnO_2$ and $MnO_2 + 2NaOH + O = Na_2MnO_4 + H_2O$. The liberated oxygen is washed with a cold alkaline solution and collected in gasometers. In this process the sodium manganate is first decomposed by the steam, giving off oxygen, while it is afterwards regenerated by taking up oxygen from the current of air passed over the residue.

In both cases, the oxygen is subsequently compressed in steel cylinders at about 1800 pounds pressure. The purity of oxygen obtained by these methods varies from 92 to 98 per cent., and even 99 per cent. purity has been produced. The Pharmacopœia demands not less than 95 per cent. purity.

Oxygen is without color, odor and taste, and is soluble in 34 times its volume of water and in 3.6 volumes of alcohol at 25° C. (77° F.). The Pharmacopœia permits traces of carbon dioxide, as shown by the test with barium hydroxide solution, and gives appropriate tests for the absence of halogens, acids, and bases. The purity percentage of the gas is directed to be determined by mixing about 50 mils. (or Cc.),

accurately measured in a calibrated tube, with 10 mils. (or Cc.) of an alkaline solution of pyrogallol (made by mixing a solution of 0.5 Gm. of pyrogallol in 2 mils. (or Cc.) of distilled water, immediately before using, with a solution of 12 Gms. of potassium hydroxide in 8 mils. (or Cc.) of distilled water), when not less than 95 per cent. of the gas should be absorbed.

Nitrogen Monoxide.—This compound, also known as nitrous oxide and as laughing gas, is the only combination of nitrogen and oxygen officially recognized. It is obtained by heating ammonium nitrate, free from chloride, to a temperature of 200° C. (392° F.) and gradually increasing the heat but not exceeding 240° C. (464° F.), when decomposition results, nitrogen monoxide and water being formed. Thus: $NH_4NO_3 = N_2O + 2H_2O$. For the purification of the gas, it is passed through solutions of potassium hydroxide and of ferrous sulphate, and is afterwards compressed in metal cylinders under pressure, in which form it is offered on the market.

Nitrous oxide is without color, but possessed of a slight odor and a sweetish taste. It is quite soluble in water at low temperatures and even at 25° C. (77° F.), water takes up 1.3 volumes of the gas. The Pharmacopœia gives appropriate tests for the possible presence of carbon dioxide, halogens, acids and bases, and reducing substances. The gas is used as an anesthetic in dentistry and minor surgery.

CHAPTER XXXVIII.

CHLORINE, BROMINE, AND IODINE.

Chlorine.—Chlorine in its elementary state is not recognized in the Pharmacopœia, but it is used occasionally by physicians in the form of an aqueous solution, known as Liquor Chlori Compositus or Compound Solution of Chlorine, and for the preparation of which the *National Formulary* gives full directions. It is considered to be a solution containing about 0.35 to 0.4 per cent. of chlorine, together with potassium chloride and some oxides of chlorine, and should be freshly prepared when wanted.

Compound solution of chlorine is intended for internal administration of chlorine, and the directions of the *National Formulary* make the extemporaneous preparation of the solution an easy task. When moderately dilute hydrochloric acid is allowed to act upon potassium chlorate, as directed in the process, a greenish-yellow gas is formed, which has been called euchlorine, and is a mixture of chlorine and chlorine dioxide. The reaction occurring may be shown by the following equation: $2KClO_3 + 4HCl = 2KCl + 2H_2O + 2ClO_2 + Cl_2$. Care is necessary in adding the distilled water in divided portions to guard against the loss of chlorine gas when inserting the stopper prior to agitating the flask. The finished solution is a liquid of almost golden-yellow color and a strong chlorine odor.

If pure chlorine water is wanted for use in chemical operations or otherwise, it may be prepared by heating pure hydrochloric acid, moderately diluted with water, in a flask with an excess of manganese dioxide in lumps of about the size of filberts, the gas evolved being passed through a small quantity of water contained in a wash bottle and then into a larger volume of distilled water kept at a temperature not above 10° C. (50° F.) until a saturated solution is obtained. The object of previously washing the gas is to remove any hydrochloric acid vapors that may have escaped along with the chlorine. Such chlorine water deteriorates rapidly when exposed to air and light, but can be preserved for short periods of time if kept in small bottles, well filled and tightly stoppered and paraffined, in a cool, dark place.

When preparing chlorine water, sulphurous acid, and similar solutions, it may happen that, owing to cessation or interruption of the gas flow, a partial vacuum is produced in the generating flask, and, as a consequence, liquid from the wash bottle is drawn over into the flask, and, coming in contact with the heated glass, will cause a fracture. This may be avoided either by using a safety tube

or by disconnecting the flask from the wash bottle as soon as gas bubbles cease to pass over.

Bromine.—Bromine is employed in its free state as an antiseptic and disinfectant, and is occasionally used internally as an alterative. It is a heavy, dark brownish-red liquid, which even at ordinary temperatures evolves a highly irritating vapor; hence considerable care is necessary in handling bromine. A vial of bromine should be well cooled before opening, especially in warm weather, to avoid accidents; and if large quantities are to be used, as in the manufacture of syrup of ferrous bromide and similar preparations, it is best to open the vial under ice water. Contact of bromine or its vapor with metallic surfaces must be carefully avoided.

The manufacture of bromine has rapidly increased during the last forty-five years, and immense quantities of it are now produced in this country. It occurs in nature, in aqueous solution, combined with sodium, magnesium, and calcium, and is present in sea water to the extent of about $\frac{1}{175}$ of 1 per cent. The commercial sources of bromine are the mother-liquors left after the crystallization of sodium chloride at the salt wells of Ohio, Pennsylvania, West Virginia, and Michigan, in this country, and near Stassfurt, in Germany. Since the bromides are far more soluble than the chlorides, the former remain in solution in the mother-liquors, to which the name bittern is given in this country. The bittern is concentrated until a density of about 1.45 is reached, which facilitates the further removal of chlorides and sulphates, then transferred to stoneware stills, where a mixture of sulphuric acid, and manganese dioxide is added, which, with the aid of heat, liberates the bromine according to the following reaction: $MgBr_2 + MnO_2 + 2H_2SO_4 = Br_2 + MgSO_4 + MnSO_4 + 2H_2O$. The bromine vapor is condensed in well cooled receivers and freed from water by distillation over calcium chloride.

Bromine is soluble in 28 parts of water at 25° C. (77° F.), but its solubility is materially increased by the presence of potassium bromide. The Pharmacopœia directs bromine water, for use as a test-solution, to be made by dissolving 1 mil. (or Cc.) of bromine in sufficient water to make 100 mils. (or Cc.) of solution. It changes readily, but is more permanent than chlorine water, and should be kept in a dark place.

It is difficult to obtain bromine entirely free from chlorine, the plan usually followed being distillation with a bromide, whereby the corresponding chloride is formed and bromine set free. The chief impurity, as stated above, is chlorine, and the equation $Ba + Cl_2 = BaCl_2$ shows that 2 atoms or 70.92 Gms. of chlorine are capable of forming 1 molecule or 208.29 Gms. of anhydrous barium chloride; hence 1 Gm. of chlorine will form 2.936+ Gms. of the salt, or 0.01 Gm. will form 0.0294 (actually 0.02936+) Gm. Advantage may be taken of this fact in determining the exact amount of chlorine in any

sample of bromine by the following method: Mix 1 Gm. of bromine with 10 mils. (or Cc.) of distilled water, adding sufficient ammonia water to produce a clear solution, then digest with barium carbonate, filter, evaporate the filtrate to dryness, and gently ignite the saline residue. The latter should be soluble in absolute alcohol, and every 0.0294 Gm. of insoluble residue will indicate 1 per cent. of chlorine, barium chloride being insoluble, while the bromide is soluble in absolute alcohol.

Iodine.—Iodine is more extensively employed in its elementary state than any other element, both internally and externally. It was formerly derived solely from the ashes of sea plants, particularly of certain species of Laminaria. These ashes are known on the coast of Scotland, where at one time the chief iodine manufactories were located as *kelp*, in Norway as *varec*, and in Spain as *barilla;* they contain iodine in the form of alkali iodides, NaI and KI. After treatment with water the chlorides, carbonates, and sulphates present are removed by evaporation of the solution and crystallization; sulphuric acid is then added to decompose sulphides and other sulphur compounds; to the acid liquid, manganese dioxide is added, and the mixture is heated. The iodine, volatilizing, passes into suitable condensing flasks and sublimes, a reaction similar to that stated under chlorine and bromine taking place.

At present vast quantities of iodine are obtained in South America from the mother-liquors of the so-called Chili saltpetre, sodium nitrate, which contains iodine in the form of sodium iodate. The iodine is obtained either by direct precipitation with sulphurous acid or sodium bisulphite and sulphur dioxide or by sublimation, after addition of manganese dioxide and sulphuric acid to cuprous iodide, which has been previously precipitated from a solution of sodium iodide by cupric and ferrous sulphates. The chemical reactions involved in these two processes can be seen from the following equations:

By direct precipitation:

$$2NaIO_3 + 3NaHSO_3 + SO_2 = 4NaHSO_4 + Na_2SO_4 + I_2.$$

By sublimation, from cuprous iodide:

(1) $NaIO_3 + 3NaHSO_3 = 3NaHSO_4 + NaI.$

(2) $2NaI + 2CuSO_4 + 2FeSO_4 = Cu_2I_2 + Na_2SO_4 + Fe_2(SO_4)_3.$

(3) $Cu_2I_2 + 2MnO_2 + 4H_2SO_4 = 2CuSO_4 + 2MnSO_4 + I_2 + 4H_2O.$

The crude iodine thus obtained is freed from moisture and purified by resublimation. Commercial iodine may contain as impurities, cyanogen, chlorine, and bromine, present as CNI, ICl_3, and IBr. The Pharmacopœia demands the absence of iodine cyanide, which is a very poisonous compound, and limits the amount of chlorine and bromine. In the official test for iodine cyanide, a further addition

of a drop of ferric chloride test-solution, made before adding the sodium hydroxide solution, would render the reaction more intense, as it depends upon the formation of ferric ferrocyanide, $Fe_4(FeC_6N_6)_3$, which, if present in sufficient quantity, will settle as a blue precipitate, otherwise only a blue color is imparted to the liquid. The official limit-test for chlorine and bromine depends upon the greater solubility of silver chloride and bromide in ammonia water and their subsequent precipitation upon the addition of nitric acid.

The Pharmacopœia requires not less than 99.5 per cent. of purity for iodine, which is volumetrically determined with tenth-normal sodium thiosulphate solution, each mil. (or Cc.) of which corresponds to 0.012692 Gm. of iodine. If 0.50 Gm. of iodine be used for the valuation, as directed in the Pharmacopœia, 39.12 mils. (or Cc.) of the thiosulphate solution will be required to decolorize the liquid completely; for 99.5 per cent. of 0.50 is equal to 0.4975, and 0.4975 divided by 0.012692 yields 39.12. The exact percentage of purity may be ascertained by multiplying the number of mils. (or Cc.) of tenth-normal sodium thiosulphate solution consumed by 1.2692 (0.012692×100) and dividing the product by the weight of iodine used in the test. The reaction involved may be explained by the following equation, $2\ (Na_2S_2O_3 + 5H_2O) + I_2 = 2NaI + Na_2S_4O_6 + 10H_2O$, sodium iodide and sodium tetrathionate being formed, both of which yield colorless solutions.

One solid and two liquid preparations containing iodine in a free state are recognized in the Pharmacopœia, namely, an alcoholic solution designated as tincture of iodine, containing 7 Gms. of iodine and 5 Gms. of potassium iodide in 100 mils. (or Cc.); an aqueous solution known as Lugol's Solution, containing 5 per cent. by weight of iodine held in solution by twice its weight of potassium iodide; and an ointment containing 4 per cent., by weight, of iodine. The amount of iodine present in any sample of the tincture or compound solution can be readily determined by titration with sodium thiosulphate. In the case of the compound solution of iodine, the Pharmacopœia requires that it shall contain not less than 4.8 per cent., nor more than 5.2 per cent. of iodine, and not less than 9.8 per cent., nor more than 10.2 per cent. of potassium iodide, which latter is determined by evaporation of 5 Gms. of the solution, accurately weighed, moistening the mass repeatedly with distilled water until finally a white residue is obtained. Tincture of iodine is required to contain not less than 0.45 Gm. nor more than 0.55 Gm. of potassium iodide in every 10 mils. (or Cc.), and in the assay for iodine content, 5 mils. (or Cc.) of the tincture must require not less than 25.6 mils. (or Cc.) nor more than 29.55 mils. (or Cc.) of tenth-normal sodium thiosulphate solution for complete decoloration, showing the presence of not less than 6.5 Gms. nor more than 7.5 Gms. of iodine in 100 mils. (or Cc.) of the tincture.

Two other liquid preparations of iodine are used by physicians,

known respectively as Churchill's tincture of iodine, and decolorized tincture of iodine; formulas for the two solutions are given in the *National Formulary*. The first-named is recognized under the title *Tinctura Iodi Fortior* or *Stronger Tincture of Iodine*, and contains in 100 mils. (or Cc.) iodine 16.5 Gms., potassium iodide 3.3 Gms., water 25 mils. (or Cc.), and sufficient alcohol to make the prescribed volume. Decolorized tincture of iodine is not a solution of iodine at all, the name being misapplied; the finished colorless product contains sodium iodide, sodium tetrathionate, and ammonium iodide, formed by reaction between iodine, sodium thiosulphate, and ammonia water. The preparation in a short time acquires a disagreeable alliaceous odor and deposits crystals of sodium tetrathionate, which may be removed by filtration.

Iodine forms with hydrogen an important compound, hydriodic acid, which in the form of a diluted solution is recognized in the Pharmacopœia, and from which in turn the official syrup of hydriodic acid is made. The diluted acid is of 10 per cent. strength; while the syrup is required by the Pharmacopœia to yield, when assayed, not less than 1.3 Gms. nor more than 1.45 Gms. of hydrogen iodide, or absolute acid, from 100 mils. (or Cc.) of the syrup. In both cases the determination is made volumetrically by means of tenth-normal silver nitrate solution, as explained under Diluted Hydriodic Acid.

CHAPTER XXXIX.

SULPHUR, PHOSPHORUS, CARBON, AND BORON.

Sulphur.—Sulphur is found widely distributed, both in a free state and in combination. It occurs most abundantly in the native state in volcanic countries. In America beds of native sulphur have been discovered in Louisiana, California, Nevada, Utah and other parts of the western United States, Mexico, the volcanic islands of Alaska, the West Indies, etc. While formerly the greater part of the sulphur used in this country came from Italy, great changes have occurred in the sulphur industry during the past 25 years, and large quantities of sulphur are now exported. The sulphur deposits of Louisiana are estimated to contain 40 million tons of sulphur beneath a layer of quicksand about 500 feet thick, and the credit of devising means for successfully bringing this sulphur to the surface belongs to Hermann Frasch, at one time a student of pharmacy in Philadelphia, who later became a chemist and devised means for desulphurizing petroleum, which brought him fame and fortune. Frasch's method for bringing the sulphur to the surface consists in melting it under ground by means of superheated water having a temperature of 160° C. (328° F.), which is forced into the sulphur deposits, and subesquently recovering the molten sulphur by means of an admixture of hot air under pressure.

The apparatus used consists of 3 concentric tubes having a diameter of 9, 6 and 3 inches respectively, suitably fixed within each other, and the whole sunk in a 10-inch well drilled through the alluvial deposit of rock and then through the sulphur deposit. The two smaller tubes are lined with aluminum, as this metal is not corroded by sulphur. The superheated water is forced under pressure of 100 pounds into the space surrounding the 6-inch tube, and near the end of the latter passes into the sulphur rapidly melting the latter, which then passes up into the second tube through perforations in this and the outer tube. In order to overcome the necessity of pumping and to facilitate the rising of the fluid sulphur, hot compressed air is passed down through the innermost tube and mixing with the fused sulphur, lowers its specific gravity, and thus allows it to be raised by the hydrostatic pressure of the water in the ground. The discharge pipe is raised about 70 feet above the ground and the molten sulphur flows into large wooden bins about 65 feet high and capable of holding over 100,000 tons of sulphur. The liquid sulphur solidifies rapidly, and as thus obtained is nearly 99.5 per cent. pure.

Large quantities of sulphur are also obtained by heating sulphur

ore in furnaces, both in Sicily and Nevada, by roasting the ore and also by passing a current of carbon dioxide into an aqueous suspension of the residues obtained in the Leblanc soda process containing calcium sulphides; in the latter case calcium carbonate and hydrogen sulphide are formed, the gas being collected and burned with an insufficient supply of air, whereby sulphur is separated.

Commercially, sulphur occurs in four varieties, namely, that known as stick or roll sulphur, chiefly used for fumigation and bleaching; and sublimed, washed, and precipitated sulphur, extensively used in medicine. Roll sulphur, known also as brimstone, is prepared by heating the crude sulphur obtained from various sources, allowing impurities to settle and pouring the fused sulphur into cylindrical moulds, in which it is allowed to congeal.

Sulphur Sublimatum, Sublimed Sulphur.—This, as its name indicates, is obtained by vaporizing sulphur and passing the vapor into large stone or brick chambers, the temperature of which is not allowed to rise above 100° or 110° C. (212° or 230° F.), where the sulphur is deposited in partly crystalline and partly amorphous particles known as *flowers of sulphur*. The two varieties can be separated from each other by treatment with carbon disulphide, which dissolves the crystalline but not the amorphous sulphur. In boiling solutions of alkali hydroxides sulphur is perfectly soluble, forming such compounds as alkali pentasulphide and thiosulphate. Nearly all sulphur is contaminated with arsenic, and this, as arsenic trisulphide, As_2S_3, together with traces of selenium and some sulphuric acid formed by oxidation, are the usual impurities found. Sublimed sulphur is practically insoluble in water and nearly insoluble in alcohol, but is soluble in chloroform and in olive oil, and freely soluble in carbon disulphide. Water shaken with it imparts an acid reaction to litmus paper.

The Pharmacopœia requires not less than 99 per cent. of purity and allows not more than 0.5 per cent. of fixed impurities upon ignition. The official assay method depends upon the conversion of the sulphur into barium sulphate, which is then well washed, dried and weighed; each Gm. of barium sulphate obtained represents 0.13730 Gm. of absolutely pure sulphur, and from its weight the purity percentage can thus be readily calculated.

Sulphur Lotum. Washed Sulphur.—This is prepared by macerating sublimed sulphur with diluted ammonia water for 3 days in a closed vessel, agitating occasionally. This treatment removes any sulphuric acid and arsenic sulphide present as ammonium sulphate, arsenite, and sulpharsenite, according to the following reaction: $H_2SO_4 + As_2S_3 + 8NH_4OH = (NH_4)_2SO_4 + (NH_4)_3AsO_3 + (NH_4)_3AsS_3 + 5H_2O$. The mixture is subsequently strained, and the resulting purified sulphur is washed with cold water to remove excess of ammonia; it is finally dried thoroughly with the aid of moderate heat, so as to prevent oxidation.

The Pharmacopœia demands that washed sulphur shall contain not less than 99.5 per cent. of pure sulphur, and that upon volatilization or ignition it shall not leave more than 0.4 per cent. of residue. When shaken with water, the latter should affect neither blue nor red litmus paper, showing the absence of both acid and ammonia. The purity percentage of washed sulphur is determined exactly as in the case of sublimed sulphur, by oxidizing the sulphur present to sulphuric acid and precipitating the latter as barium sulphate, which is then well washed, dried and weighed.

Sulphur Præcipitatum. Precipitated Sulphur.—This variety of sulphur, also known as *milk of sulphur* (*lac sulphuris*), is made from sublimed sulphur by first uniting this to an alkali and then decomposing the resulting compound with an acid. Milk of lime is preferred mainly on account of its cheapness; upon boiling it with sulphur both pentasulphide and thiosulphate are obtained in solution, thus: $12S + 3CaO = 2CaS_5 + CaS_2O_3$. The Pharmacopœia directs that hydrochloric acid shall be added to the clear filtrate until the latter is nearly neutralized, but still exhibits an alkaline reaction; this is partly to avoid decomposition of the calcium thiosulphate, which would yield sulphur insoluble in carbon disulphide and in a coarser state of division, and partly to prevent the precipitation of any arsenic trisulphide, for, if arsenic had been present in the sublimed sulphur, it would have formed calcium sulpharsenate, $Ca_3As_2S_8$, which is soluble in the alkaline liquid, but is decomposed by acids. The official process causes a decreased yield of precipitated sulphur, but a purer product, the final reaction being only between the calcium pentasulphide and hydrochloric acid. Sulphuric acid is sometimes used in place of hydrochloric acid, but is not permissible, since it would contaminate the sulphur with insoluble calcium sulphate, whereas hydrochloric acid yields calcium chloride, easily removable by washing.

The Pharmacopœia requires not less than 99.5 per cent. of purity and not more than 0.3 per cent. of fixed impurities, upon ignition. The percentage purity is determined by conversion of the sulphur into barium sulphate, as stated under Sublimed Sulphur.

Sulphur Iodide.—Sulphur iodide, at one time prescribed by physicians in the form of an ointment, is no longer recognized in the Pharmacopœia, but a method for its preparation is given in the *National Formulary*, identical with the former official directions, thus: 1 part of washed sulphur and 4 parts of iodine are mixed in a flask and gradually heated in a waterbath to 60° C. (140° F.), the heat being then increased to 100° C. (212° F.) until perfect fusion has taken place. The resulting product is in all probability not a definite chemical compound, although formerly looked upon as sulphur monoiodide, as alcohol will abstract the iodine and even boiling water is capable of causing elimination of all the iodine. Sulphur iodide must be preserved in well stoppered bottles.

Phosphorus.—Phosphorus occurs in nature chiefly as calcium phosphate, which makes up the structure of bone and is found as extensive mineral deposits. Pure phosphorus is obtained by distilling calcium metaphosphate with sand and charcoal. Owing to its great avidity for oxygen and ready inflammability, it must be preserved under water, and care is necessary in handling it. Elementary phosphorus is used to a considerable extent in medicine, in the form of an official and other pills. The elixir and spirit of phosphorus are no longer recognized in the Pharmacopœia; neither is phosphorated oil.

Carbon.—Carbon is recognized in the Pharmacopœia only in the form of wood charcoal, and will be considered in connection with the product of woody fiber (see Cellulose). Animal charcoal is no longer official, but is extensively employed as a decolorizing agent by manufacturing chemists; it is prepared by roasting bones in iron cylinders until vapors cease to be given off; the residuary charcoal, mixed with large proportions of inorganic constituents, is known in its crude state as bone-black. Meat and blood are also made to yield animal charcoal by a somewhat similar process. Purified animal charcoal differs from crude bone-black in having been repeatedly treated with boiling diluted hydrochloric acid, whereby all acid-soluble impurities, such as calcium carbonate and phosphate, are removed. By this treatment animal charcoal loses about 80 per cent. in weight, leaving a small proportion (4 per cent.) of siliceous matter mixed with the purified charcoal. If not completely carbonized, animal charcoal will impart color to water if boiled with the same in the presence of potassium hydroxide. The remarkable decolorizing property of animal charcoal is due to the very fine state of division of the carbon and its consequent increased surface attraction. While crude animal charcoal is largely used for neutral solutions in the arts, only the purified article should be employed for acid liquids or delicate chemical solutions. So-called spent charcoal, charged with organic matter, can be regenerated by appropriate heating.

The only preparation of carbon to be considered is carbon disulphide, CS_2, which is not employed medicinally, but is a valuable solvent for caoutchouc, fats, and many other substances. It is prepared by direct union of charcoal and sulphur, vapors of the latter being passed over the former heated to redness, and then condensed in suitable receivers. It is freed from dissolved sulphur by distillation on a water-bath, while hydrogen sulphide, which is also formed, is removed by agitation with mercury; the liquid is further rectified by distillation with wax or fat, whereby certain offensive sulphur compounds are removed. When exposed to light, carbon disulphide assumes a yellow color and acquires a fetid odor, owing to decomposition.

Boron.—Boron is never used in pharmacy or medicine in its free state. Its compound with oxygen, boric acid, will be considered in the following chapter.

CHAPTER XL.

THE INORGANIC ACIDS.

INORGANIC acids, which are extensively employed by pharmacists, and therefore of great importance, are combinations of non-metallic elements with hydrogen and oxygen, and in a few cases with hydrogen alone. The presence of hydrogen lends to these compounds their peculiar acid character. Compounds with oxygen only, possess no acid properties, and are termed anhydrides or simply oxides; they, however, unite chemically with water to form well defined acids; thus we have sulphurous and sulphuric anhydrides, SO_2 and SO_3, known also as sulphur dioxide and trioxide, which, combining with water yield sulphurous and sulphuric acids, as $SO_2 + H_2O = H_2SO_3$ and $SO_3 + H_2O = H_2SO_4$; carbon dioxide, CO_2, in contact with water, yields carbonic acid, H_2CO_3; nitric anhydride, or nitrogen pentoxide, N_2O_5, yields nitric acid, HNO_3, thus $N_2O_5 + H_2O = 2HNO_3$; phosphoric anhydride or phosphorus pentoxide, P_2O_5, will yield with water phosphoric acid, H_3PO_4, thus $P_2O_5 + 3H_2O = 2H_3PO_4$, etc.

Acids are characterized by a sour taste, the property of changing the color of blue litmus paper to red, of neutralizing alkalies, and of forming with these and other bases well defined salts. The salts thus formed are not always neutral compounds, which fact is due to different basicity of the various acids, depending upon the number of replaceable hydrogen atoms present in the acid; hence the terms mono-, di-, tri-, and tetrabasic acids, referring to the presence of 1, 2, 3, or 4 atoms of hydrogen, which can be replaced by as many basylous atoms or groups, giving rise to normal and acid salts. Normal salts are such as are formed by complete saturation of an acid by a base, or, in other words, they are produced whenever all the replaceable hydrogen of an acid is replaced by a base; acid salts, on the other hand, still retain a part of the replaceable hydrogen of acids, and are the result of imperfect neutralization of an acid by a base. (Examples, KNO_3 and Na_2SO_4 are normal salts, while $NaHCO_3$ and KH_2PO_4 are acid salts.) Monobasic acids never form acid salts. In the pharmacopœial chemical formulas for inorganic acids the replaceable hydrogen is stated first, hence the basicity of the acid can be seen at a glance; thus hydriodic, hydrochloric, hydrobromic, hypophosphorous, and nitric acids are all monobasic, sulphuric acid is dibasic, while boric and phosphoric acids are tribasic.

Both crude and purified acids are offered for sale by manufacturers; the former, while suitable for many technical purposes, should never be used for pharmaceutical preparations. A very important point in

connection with inorganic acids is the percentage of hydrogen compound, or so-called absolute acid, present in the commercial solutions sold under their respective names. The Pharmacopœia, in every instance, designates the percentage strength of the official acids, and pharmacists should insist on being furnished such acids by manufacturing chemists; the designation C. P. (chemically pure), placed on the labels of acid bottles, is no clue as to the strength of the solution; either the initials U. S. P. or the percentage of absolute acid should be stated. Manufacturing chemists will not be slow in recognizing the justice of such a demand if pharmacists insist upon it; otherwise the same uncertainty as to strength will continue. All working formulas of the Pharmacopœia, requiring the use of inorganic acids, are based upon the assumption that acids of official strength will be used. Absolute purity is not demanded for official acids, for, while this is essential for chemical reagents, it is considered unnecessary for medicinal acids and, if insisted upon, would greatly enhance the cost of the article without adding to the value of the acid for medicinal or pharmaceutical purposes. Certain impurities, which it would be difficult to remove entirely except at considerable expense, are allowed by the Pharmacopœia to be present within prescribed limits. As different acids have different saturating powers, the official volumetric determinations are only useful in fixing the strength of the acid examined, after the absence of other acids has been proved by the tests prescribed for that purpose.

Only such inorganic acids will be considered here as are designated in the Pharmacopœia, and are therefore of special interest to the student of pharmacy. Details of the manufacture of the principal acids will not be essayed, as text-books on chemistry furnish all such information. While there must naturally exist a great diversity in the strength of the various so-called strong acids, the Pharmacopœia has fixed the proportion of absolute acid in all official diluted inorganic acids at not less than 9.5 per cent., nor more than 10.5 per cent., with the exception of diluted nitrohydrochloric acid. With one exception, boric acid, all the official inorganic acids are liquid.

The following is a list of the official inorganic acids:

English name.	Latin name.
Boric Acid,	Acidum Boricum.
Diluted Hydriodic Acid,	Acidum Hydriodicum Dilutum.
Diluted Hydrobromic Acid,	Acidum Hydrobromicum Dilutum.
Hydrochloric Acid,	Acidum Hydrochloricum.
Diluted Hydrochloric Acid,	Acidum Hydrochloricum Dilutum.
Hypophosphorous Acid,	Acidum Hypophosphorosum.
Diluted Hypophosphorous Acid,	Acidum Hypophosphorosum Dilutum.
Nitric Acid,	Acidum Nitricum.
Nitrohydrochloric Acid,	Acidum Nitrohydrochloricum.
Diluted Nitrohydrochloric Acid,	Acidum Nitrohydrochloricum Dilutum.
Phosphoric Acid,	Acidum Phosphoricum.
Diluted Phosphoric Acid,	Acidum Phosphoricum Dilutum.
Sulphuric Acid,	Acidum Sulphuricum.
Aromatic Sulphuric Acid,	Acidum Sulphuricum Aromaticum.
Diluted Sulphuric Acid,	Acidum Sulphuricum Dilutum.

Boric Acid. H_3BO_3 or $B(OH)_3$.—Boric acid, also known as boracic acid, occurs in nature both in a free and combined state, the free acid, in the form of vapor, issuing with steam from the earth in volcanic regions, particularly in Tuscany, Italy, while the combined acid is usually found as sodium tetraborate or borax. Medicinal boric acid is probably all obtained by decomposition of a boiling solution of borax with hydrochloric acid, which latter is preferable to sulphuric acid, as it can be more readily removed from the crystals of boric acid by washing; the reaction is a very simple one—$(Na_2B_4O_7 + 10H_2O) + 2HCl = 4H_3BO_3 + 2NaCl + 5H_2O$. When heated, boric acid gradually loses water and is converted into metaboric acid, HBO_2; with increasing temperature, into tetraboric acid, $H_2B_4O_7$; and, finally, above 160° C. (320° F.) all hydrogen is eliminated in the form of water and boron trioxide remains, thus $2H_3BO_3 = B_2O_3 + 3H_2O$.

Its chief characteristics are that it imparts a green color to the flame of burning alcohol, and that it changes the yellow color of turmeric paper to reddish-brown even in the presence of hydrochloric acid, which color is further changed to greenish-black by addition of ammonia water.

The Pharmacopœia requires that when dried to constant weight in a desiccator over sulphuric acid, boric acid shall contain not less than 99.5 per cent. of absolute hydrogen borate, to be determined by dissolving about 2.5 Gms. of the acid in a mixture of 50 mils. (or Cc.) each of distilled water and glycerin, and then titrating the solution with normal sodium hydroxide solution in the presence of phenolphthalein as indicator.

Diluted Hydriodic Acid.—An aqueous solution containing 10 per cent. (not less than 9.5 per cent., nor more than 10.5 per cent., U. S. P.) of hydrogen iodide, HI, and about 0.63 per cent. of hydrogen hypophosphite, HPH_2O_2. It may be conveniently prepared by the official formula, which involves the decomposition of potassium iodide and hypophosphite by means of tartaric acid in hydro-alcoholic solution. The reaction is shown by the following equation: $KI + KPH_2O_2 + 2H_2C_4H_4O_6 = HI + HPH_2O_2 + 2KHC_4H_4O_6$, from which it will be seen that 166.02 parts of potassium iodide are capable of yielding 127.93 parts of hydrogen iodide, and 104.156 parts of potassium hypophosphite are capable of yielding 66.064 parts of hydrogen hypophosphite; hence the quantities of the two salts ordered in the official formula, 135 Gms. of potassium iodide and 10 Gms. of potassium hypophosphite should yield 104.02 Gms. and 6.3428 Gms. of hydrogen iodide and hydrogen hypophosphite respectively. The use of alcohol in the process materially aids in the precipitation of the newly formed acid potassium tartrate, as does also the application of cold, the Pharmacopœia allowing not more than 0.0055 Gm. of residue upon evaporation of 5 mils. (or Cc.) of the diluted acid to dryness and subsequent ignition. Upon evaporation of the filtrate for removal of

the alcohol it assumes a yellowish color when concentrated, but no iodine is liberated, and the liquid again becomes colorless when diluted with distilled water.

In the official assay all the hydriodic acid present is precipitated by tenth-normal silver nitrate solution added in excess, which excess is determined by subsequent titration with tenth-normal potassium sulphocyanate solution in the presence of some nitric acid, ferric ammonium sulphate being used as an indicator. Since each mil. (or Cc.) of the silver solution, containing 0.016989 Gm. of silver nitrate, is capable of precipitating 0.012793 Gm. of hydrogen iodide, as shown by the equation $AgNO_3 + HI = AgI + HNO_3$, not less than 37 nor more than 41 mils. (or Cc.) of tenth-normal silver nitrate solution will be required to indicate conformity with the official requirement, if 5 Gms. of the diluted acid be taken for the assay. The addition of nitric acid is made to prevent the discoloration of the liquid by the indicator. The latter shows a permanent reddish-brown color of ferric sulphocyanate immediately when all excess of silver nitrate has been precipitated as silver sulphocyanate.

Solutions of hydriodic acid decompose readily, especially when exposed to light, but such change is obviated by the presence of small quantities of hypophosphorous acid. In the author's experience diluted hydriodic acid made by the official method has kept perfectly for over six months in diffused light.

Diluted Hydrobromic Acid.—An aqueous solution containing 10 per cent. (not less than 9.5 per cent., nor more than 10.5 per cent., U. S. P.) of absolute hydrogen bromide, HBr, which latter is a rather unstable gaseous compound. The medicinal acid is prepared by manufacturers usually of two strengths, 34 per cent. and 10 per cent., the former being the more economical article to purchase, as the requisite proportion of water to reduce it to the official acid can be easily added by the pharmacist, 10 Gms. of 34 per cent. acid mixed with 24 Gms. of distilled water yielding 34 Gms. of 10 per cent. acid. Hydrobromic acid can be obtained in several ways, a very convenient method being the following: Moderately diluted sulphuric acid is poured slowly, and with constant stirring, into a hot saturated solution of potassium bromide, when the following decomposition takes place: $2KBr + H_2SO_4 = 2HBr + K_2SO_4$; after twenty-four hours the potassium sulphate has crystallized out, the solution of hydrobromic acid is poured off, and the crystals are slowly washed with ice-cold water to recover adhering acid. Finally, the acid liquid is distilled in a glass retort on a sandbath nearly to dryness. Its strength is ascertained by titration with normal potassium hydroxide solution, and sufficient water is then added to produce either a 34 or 10 per cent. solution as desired.

For preparing small quantities of the official acid, the precipitation methods of Wade and Fothergill may be employed, which are based

on the decomposition of potassium bromide with tartaric acid; thus $KBr + H_2C_4H_4O_6 = HBr + KHC_4H_4O_6$. 11.9 Gms. of potassium bromide and 15 Gms. of tartaric acid are each dissolved in 30 mils. (or Cc.) of cold distilled water, the acid solution is poured into the saline solution, and the mixture, after having been well shaken for five or ten minutes, is placed in ice water or an ice chest for twenty-four or thirty-six hours; it is then filtered, and the vessel and filter carefully washed with ice water until the filtered liquid weighs 81 Gms. A small quantity of acid potassium tartrate is likely to remain in the diluted acid prepared by this method.

The official acid has a specific gravity of about 1.076 at 25° C. (77° F.). The Pharmacopœia excludes all impurities except slight traces of sulphuric acid and chlorides, and directs that about 20 mils. (or Cc.) of the diluted acid, accurately weighed, be mixed with 30 mils. (or Cc.) of distilled water and then titrated with normal potassium hydroxide solution, using methyl orange test-solution as indicator. Since each mil. (or Cc.) of normal alkali solution corresponds to 0.08093 Gm. of hydrogen bromide, the number of mils. required to neutralize 5 Gms. of diluted hydrobromic acid should be not less than 5.85 nor more than 6.5 to insure conformity with the official standard.

Hydrochloric Acid.—An aqueous solution of hydrogen chloride, HCl. This acid may be prepared quite pure by decomposing sodium chloride with pure sulphuric acid and conducting the gas into water. The crude acid of commerce is often obtained as a by-product in the manufacture of sodium or potassium carbonates from the respective chlorides; since sulphates are first made in this process by acting on the chlorides with sulphuric acid, the reactions are the same in the manufacture of crude and pure acid, and possibly occur in two distinct steps, namely: 1. $NaCl + H_2SO_4 = HCl + NaHSO_4$. 2. $NaCl + NaHSO_4 = HCl + Na_2SO_4$. The crude acid of commerce, better known as muriatic acid, is often of a deep-yellow color, owing to organic matter and traces of iron in solution; it should not be employed for pharmaceutical preparations.

Official hydrochloric acid should be free from all impurities except a bare trace of non-volatile substances and arsenic, the latter derived in all probability from the sulphuric acid. It has a specific gravity of about 1.155 at 25° C. (77° F.), and should contain 32 per cent. (not less than 31 per cent., nor more than 33 per cent., U. S. P.) by weight of absolute HCl, which is determined by titration with normal KOH solution. As it is more convenient to measure small quantities of strong hydrochloric acid, the Pharmacopœia directs that about 3 mils. (or Cc.) be weighed accurately in a stoppered weighing bottle, diluted with 50 mils. (or Cc.) of water and then titrated, methyl orange being used as an indicator. As each mil. (or Cc.) of the normal alkali solution is capable of neutralizing 0.03647 Gm. of hydrogen chloride, the number of mils. (or Cc.) required in the official assay,

when multiplied by 3.647 (0.03647 × 100) and then divided by the weight of the acid taken, will express the percentage of hydrogen chloride, or absolute acid, present in the sample.

Strong hydrochloric acid usually causes white fumes when exposed to the air, due to the moisture in the air, and if ammonia be present white fumes of ammonium chloride will also be formed.

Diluted Hydrochloric Acid.—It is made from the official acid by mixing it with distilled water, in the proportion of 10 parts of the former to 22 parts of the latter, by weight, or, as the Pharmacopœia gives it, 100 Gms. of the acid with 220 Gms. of distilled water. This must yield a liquid containing not less than 9.5 per cent., nor more than 10.5 per cent. of absolute HCl, for the 100 Gms. of official hydrochloric acid contain from 31 to 33 per cent. of HCl. Diluted hydrochloric acid has a specific gravity of about 1.049 at 25° C. (77° F.), and corresponds in all its properties, reactions, and tests to the official stronger acid, except that it is odorless and produces no fumes when exposed to the air, and that each Gm. of the diluted acid requires from 2.6 to 2.9 mils. (or Cc.) of normal alkali solution for complete neutralization.

Hypophosphorous Acid.—The official acid liquid recognized under this name is an aqueous solution containing about 31 per cent. (not less than 30 per cent., nor more than 32 per cent., U. S. P.) of hydrogen hypophosphite, HPH_2O_2. It may be prepared by decomposing a solution of calcium hypophosphite with oxalic acid, or by mixing a strong aqueous solution of potassium hypophosphite with a hydro-alcoholic solution of tartaric acid. The equation $KPH_2O_2 + H_2C_4H_4O_6 = HPH_2O_2 + KHC_4H_4O_6$ shows that one molecule or 104.16 parts of absolute (or 106.29 parts of the official 98 per cent.) potassium hypophosphite will yield one molecule or 66.064 parts of hydrogen hypophosphite, and hence to make 100 Gms. of the 31 per cent. acid will require 49.9 Gms. of the official potassium salt and 70.4 Gms. of tartaric acid, the former being dissolved in 50 mils. (or Cc.) of distilled water, and the latter in 100 mils. (or Cc.) of diluted alcohol. The mixture is well shaken and placed in an ice bath for several hours and then filtered, the precipitated acid potassium tartrate being well washed with diluted alcohol. After concentration of the filtrate and washings to remove the alcohol, sufficient distilled water is added to bring the weight of the cold liquid up to 100 Gms.

Official hypophosphorous acid is a colorless liquid having a specific gravity of 1.130 at 25° C. (77° F.). Its strength is determined by titration with normal potassium hydroxide solution, each mil. (or Cc.) of which corresponds to 0.06606 Gm. of the hydrogen hypophosphite, methyl orange being used as an indicator. Five Gms. of the official acid requires not less than 22.7 nor more than 24.2 mils. (or Cc.) of normal potassium hydroxide solution for neutralization.

This stronger acid is used almost entirely for manufacturing purposes and for the preparation of the official diluted acid, and it is necessary to guard against confusion of the two liquids. Manufacturing chemists have also placed on the market hypophosphorous acid containing 50 per cent. of the absolute acid.

Diluted Hypophosphorous Acid.—This acid solution is of only one-third the strength of the preceding and is directed by the Pharmacopœia to be made by mixing 1 part by weight of the 31 per cent. hypophosphorous acid with 2 parts by weight of water, and will then contain from 9.5 to 10.5 per cent. of hydrogen hypophosphite, HPH_2O_2. Its specific gravity is about 1.042 at 25° C. (77° F.) and it corresponds in all respects with the stronger acid, except that, if titrated with normal alkali solution as stated above under the stronger acid, 5 Gms. of the diluted acid will require not less than 7.2 nor more than 8 mils. (or Cc.) of the latter solution for neutralization. The chief use of this acid in pharmacy is as a preservative in certain chemical solutions prone to change by oxidation, such as diluted hydriodic acid, syrup of ferrous iodide, etc., as it possesses strong reducing properties.

Nitric Acid.—When potassium or sodium nitrate is treated with sulphuric acid, nitric acid is liberated, and may be condensed in suitable receivers. The reaction, in the case of potassium nitrate, occurs as follows: $KNO_3 + H_2SO_4 = HNO_3 + KHSO_4$; in the case of Chili saltpetre, provided a sufficient quantity of sodium nitrate be used, two distinct reactions may be said to occur, namely: 1. $NaNO_3 + H_2SO_4 = HNO_3 + NaHSO_4$; 2. $NaHSO_4 + NaNO_3 = HNO_3 + Na_2SO_4$. Sodium nitrate affords a larger yield than potassium nitrate, since the acid sodium sulphate reacts with the undecomposed nitrate at a much lower temperature than the acid potassium sulphate, the latter requiring a temperature at which the nitric acid is likely to be decomposed.

The Pharmacopœia demands absolute purity for nitric acid. If exposed to sunlight, the acid soon undergoes decomposition, a red color being imparted to the liquid, due to the formation of nitrogen tetroxide, N_2O_4; hence the acid must be kept in a dark place. Nitric acid of different strengths is placed upon the market by manufacturing chemists, ranging from 1.21 to 1.50 specific gravity; hence care is necessary to obtain the only kind recognized by the Pharmacopœia, which contains about 68 per cent. (not less than 67 per cent., nor more than 69 per cent., U. S. P.) of hydrogen nitrate, HNO_3, and has a specific gravity of 1.403 at 25° C. (77° F.), otherwise considerable annoyance may be experienced when nitric acid is to be used as an oxidizing agent in any of the official preparations.

Nitric acid, being the most corrosive of the official acids, requires care in handling; in contact with the skin, it acts chemically on the

same and produces a deep-yellow stain, this behavior, characteristic of nitric acid with albuminoid substances, being known as the xanthoproteic reaction.

The strength of nitric acid is determined as in the case of hydrochloric acid, each mil. (or Cc.) of normal potassium hydroxide solution corresponding to 0.06302 Gm. of hydrogen nitrate; hence each Gm. of official nitric acid will require from 10.63 to 10.95 mils. (or Cc.) of normal alkali solution for neutralization.

The so-called nitrous acid of commerce is simply nitroso-nitric acid —that is, nitric acid containing variable amounts of nitrogen tetroxide.

Nitrohydrochloric Acid.—This preparation, which is also known as nitromuriatic acid, is not of a definite chemical composition, and is defined by the Pharmacopœia to be a strong aqueous solution containing hydrochloric and nitric acids, nitrosyl chloride and chlorine. When strong nitric and hydrochloric acids are brought into contact, mutual decomposition takes place, the composition of the finished product depending upon the proportions of the acids used and the temperature at which they have been mixed. The Pharmacopœia directs 18 volumes of nitric acid and 82 volumes of hydrochloric acid, and, when so mixed, the following reactions probably take place: $HNO_3 + 3HCl = NOCl + Cl_2 + 2H_2O$ and $2HNO_3 + 6HCl = 2NOCl_2 + Cl_2 + 4H_2O$, nitrosyl mono- and dichloride and water being formed, while chlorine is liberated. The mixture is at first colorless, but as reaction progresses an orange-red color is developed and effervescence is observed; the best plan is to pour the two acids into a capacious bottle provided with a glass stopper and place the same in a cool dark place, gently agitating the liquid about once in 24 hours until reaction is complete, which is indicated by cessation of effervescence and the assumption of a green-yellow color. The acid liquid should then be preserved in half-filled amber glass-stoppered bottles in a cool place. This preparation should never be made extemporaneously, as accidents may result from such a proceeding, and sufficient time must be allowed for the completion of the chemical changes.

Nitrohydrochloric acid should not be dispensed if the addition of 1 drop of the acid to 1 mil. (or Cc.) of potassium iodide solution (1 Gm. in 5 mils.) does not immediately cause liberation of iodine. The acid is also known as chloro-nitrous acid and aqua regia, and owes its power of dissolving gold to the free chlorine and feeble chlorine compounds present.

Diluted Nitrohydrochloric Acid.—This solution is of nearly one-fourth the strength of the stronger acid, about 22.2 per cent., and is prepared in exactly the same manner, the diluent, distilled water, not being added until effervescence has ceased. The British Pharmacopœia prepares this acid by mixing the stronger acids at once with the

water and setting the mixture aside for fourteen days. Conflicting views exist regarding the composition of the finished product, some authorities contending that, when made by diluting the strong acids at once with water, the same reactions will occur as in a mixture of the acids alone, except that the decomposition is more gradual, while others assert that little or no change will take place, and that, in fact, the decomposed strong acids will be again restored to their original condition upon the addition of water, nitric and hydrochloric acids being regenerated. Certain it is that the diluted nitrohydrochloric acid differs from the strong acid in being free from color and possessing only a faint odor of chlorine when freshly made, which is gradually lost. The author has never observed any effervescence or change of color or odor upon mixing the strong acids direct with water and allowing the mixture to stand.

Diluted nitrohydrochloric acid should not be dispensed if 5 drops of the acid fail to liberate iodine immediately when added to 1 mil. (or Cc.) of potassium iodide solution (1 Gm. in 5 mils.).

Phosphoric Acid.—The official acid is a dense syrupy liquid containing about 86.5 per cent. (not less than 85 per cent., nor more than 88 per cent., U. S. P.) of hydrogen orthophosphate, H_3PO_4 or $PO(OH)_3$, and has a specific gravity of about 1.72 at 25° C. (77° F.). Medicinal phosphoric acid should all be made direct from phosphorus; usually oxidation by means of nitric acid is resorted to, each part of phosphorus requiring about $3\frac{1}{2}$ parts of absolute nitric acid for complete conversion, according to the following equation: $5HNO_3 + P_3 + 2H_2O = 3H_3PO_4 + 5NO$.

In order to control the reaction, about an equal weight of water is mixed with a portion of the nitric acid contained in a flask, the phosphorus is added, and the whole heated on a waterbath; when the reaction slackens, the remainder of the nitric acid is added, undiluted, small portions at a time, and the heat is continued until all the phosphorus is dissolved, after which the liquid is heated in a porcelain dish, on a sandbath, at a temperature not exceeding 190° C. (374° F.), until all traces of nitric acid have been removed. The object of limiting the temperature is to avoid conversion of the orthophosphoric acid into pyrophosphoric acid, which occurs at 200° C. (392° F.) and over. Phosphorus is frequently contaminated with arsenic, which is best removed, at this stage of the process, by diluting the acid liquid with water, passing a stream of hydrogen sulphide through it for several hours and afterward setting the liquid aside for twenty-four hours to allow the arsenic sulphide to subside. After filtration the excess of gas is removed by heating and the liquid evaporated to the desired density, every 100 Gms. of phosphorus used yielding about 370 Gms. of official phosphoric acid. This is essentially the modified process suggested some years ago by the late Dr. Squibb.

In 1875, Markoe proposed the following process, which has since

then been used with marked success on a large scale: 900 Gms. of phosphorus are placed in a stone jar and covered with 5400 Gms. of water, after which 10 Gms. of iodine are added and the mixture stirred so as to bring the iodine into contact with the phosphorus. From a glass-stoppered burette or funnel 60 Gms. of bromine are now added, drop by drop, in such a manner that the bromine shall strike the phosphorus as it falls below the water. Phosphorus pentaiodide and pentabromide, PI_5 and PBr_5, chiefly the latter, are formed by direct union, and when the reaction has ceased 5400 Gms. of nitric acid are added, the jar is placed in cold water or surrounded with ice, to control the rate of oxidation, and set aside until solution of the phosphorus has been effected. The acid liquid is then evaporated and treated as above. The phosphorus iodide and bromide are decomposed by the water present, forming phosphoric, hydriodic, and hydrobromic acids; the last two are decomposed by the nitric acid regenerating iodine and bromine with the liberation of nitric oxide. These reactions, continuing until all the phosphorus has been converted into phosphoric acid, may be expressed by the following equations: 1. $PI_5 + 5PBr_5 + 24H_2O = 6H_3PO_4 + 5HI + 25HBr$; 2. $HI + 5HBr + 2HNO_3 = I + 5Br + 2NO + 4H_2O$. The process can be conducted with bromine alone, but the presence of iodine has been found to modify the action between the phosphorus and bromine.

The impurities likely to be met with in phosphoric acid can, as a rule, be avoided in the process of manufacture, phosphorous acid being due to insufficient oxidation, while meta- and pyrophosphoric acids arise from the use of excessive heat.

Phosphoric acid made from phosphorus should be miscible with tincture of ferric chloride in all proportions, but, if made from glacial phosphoric acid, it causes turbidity, which is in part due to the presence of sodium metaphosphate in the glacial acid.

The official method of assaying phosphoric acid depends upon the precipitation of the latter as trisilver phosphate by means of silver nitrate solution. A definite quantity (about 1 Gm. accurately weighed) of the acid is first diluted with distilled water and neutralized with a solution of sodium hydroxide free from chlorides, forming secondary sodium phosphate. To a portion of this solution an excess of tenth-normal silver nitrate solution is then added, and also sufficient zinc oxide, free from chlorides, to render the liquid neutral to litmus. After filtration, the excess of silver nitrate solution is determined in one-half of the filtrate, representing one-twentieth of the weight of phosphoric acid originally taken, by titration with tenth-normal potassium sulphocyanate solution to a permanent red color. In order to insure complete precipitation of the trisilver phosphate, it is essential that a perfectly neutral liquid be employed and hence the addition of zinc oxide to neutralize the liberated nitric acid. The different reactions occurring during the assay process may be indicated by the following equations: $H_3PO_4 + 2NaOH = Na_2HPO_4 + 2H_2O$; $Na_2HPO_4 +$

$3AgNO_3 = Ag_3PO_4 + 2NaNO_3 + HNO_3$; $2HNO_3 + ZnO = Zn(NO_3)_2 + H_2O$; $AgNO_3 + KCSN = AgCSN + KNO_3$.

As each mil. (or Cc.) of tenth-normal silver nitrate solution corresponds to 0.0032687 Gm. of hydrogen orthophosphate, H_3PO_4, the difference between 25 (the number of mils., or Cc., of silver nitrate solution represented in one-half of the filtrate) and the number of mils. (or Cc.) of tenth-normal potassium sulphocyanate solution required, when multiplied by 0.32687 (0.0032687×100) and divided by one-twentieth of the weight of phosphoric acid originally taken will express the percentage of hydrogen orthophosphate present in the sample of acid.

The value of a volumetric assay of phosphoric acid with solution of alkali hydroxide depends largely upon the indicator employed; complete neutralization is not feasible, since the normal alkali phosphate itself gives an alkaline reaction. Phosphoric acid is tribasic, and, therefore, capable of forming three different compounds with the alkalies, namely, KH_2PO_4, K_2HPO_4, and K_3PO_4; the last named salt is alkaline to all color indicators, whereas the other two are either acid, alkaline, or neutral to different indicators. With phenolphthalein, KH_2PO_4 shows an acid reaction, but K_2HPO_4 a neutral reaction, but with methyl orange and congo red, KH_2PO_4 already shows a neutral reaction, and K_2HPO_4 an alkaline reaction.

Diluted Phosphoric Acid.—It is made from the preceding acid by dilution with distilled water in the proportion of 1 part by weight of the strong acid and 7.65 parts of water, or 100 Gms. and 765 Gms. respectively. Officially diluted phosphoric acid contains not less than 9.5 per cent. nor more than 10.5 per cent. of hydrogen orthophosphate, H_3PO_4, and has a specific gravity of about 1.057 at 25° C. (77° F.).

The Pharmacopœia directs the assay to be made as in the case of the strong acid, by precipitation as trisilver phosphate by means of tenth-normal silver nitrate solution.

Sulphuric Acid.—The manufacture of this acid is carried on extensively in this country and in Europe, in specially constructed leaden chambers, so arranged that the fumes from burning sulphur or iron pyrites are brought into intimate contact with steam and nitric acid vapor. Nitrogen trioxide is generated and combines with more sulphur dioxide, aqueous vapor, and atmospheric oxygen, forming nitrosulphuric acid, which, coming into contact with water, is decomposed, yielding sulphuric acid and nitrogen trioxide, and this in turn, again unites with more sulphur dioxide, etc. The following equations will explain the various steps in the process:

(1) $2SO_2 + 2HNO_3 + H_2O = 2H_2SO_4 + N_2O_3$.
(2) $N_2O_3 + 2SO_2 + O_2 + H_2O = 2SO_2OHNO_2$.
(3) $2SO_2OHNO_2 + H_2O = 2H_2SO_4 + N_2O_3$.

The foregoing are the chief reactions involved in the manufacture of sulphuric acid, which condenses and is dissolved in the water covering the floor of the leaden chambers, thus forming a dilute acid which gradually becomes more concentrated. Sulphuric acid thus obtained is usually designated as chamber acid and contains about 67 per cent. of H_2SO_4; it may be concentrated to about 78 per cent. by evaporation in leaden pans, and still further by distillation in gold-lined platinum retorts.

In order to avoid subsequent evaporation, highly concentrated sulphuric acid, 98 per cent., is now extensively manufactured in this country and abroad by the so-called contact process, which consists in bringing a mixture of sulphur dioxide and air into contact with platinized asbestos, iron oxide, or other catalyzers, which latter bodies induce a union of SO_2 with oxygen, thus forming SO_3. An important feature of the process is the purification of the furnace gases, especially the removal of arsenic and dust, the latter of which is apt to form a coating on the catalyzer and interfere with its activity. Arsenic is usually eliminated by what is known as Knietsch's method of blowing steam into the gas mixture. A large contact process plant with a daily capacity of nearly 8 tons of sulphuric acid, located at the U. S. Naval Proving Grounds, Indian Head, Md., now uses Louisiana brimstone in preference to pyrites, and employs as a catalytic agent anhydrous magnesium sulphate carrying one-fifth of 1 per cent. of metallic platinum in a finely divided state.

Crude sulphuric acid is often colored, and contains nitric and sulphurous acids and lead, the latter being readily detected by simple dilution with water. Arsenic is almost invariably present, and thus is transferred to other substances in the manufacture of which sulphuric acid is used, as hydrochloric and nitric acids, phosphorus, etc.

When sulphuric acid is mixed with water or alcohol, heat is developed and the volume of the mixture is invariably contracted. Official sulphuric acid is of oily consistence, and has a specific gravity of 1.830 at 25° C. (77° F.). It should be free from lead and other mineral impurities, but slight traces of arsenic, nitric, nitrous, and sulphurous acids are permitted. The Pharmacopœia requires the presence of not less than 93 per cent. nor more than 95 per cent. of hydrogen sulphate, H_2SO_4, and, as sulphuric acid is bibasic, the following reaction takes place when potassium hydroxide is added to complete neutrality: $H_2SO_4 + 2KOH = K_2SO_4 + 2H_2O$. Each mil. (or Cc.) of normal KOH solution, containing 0.05611 Gm. KOH, is equivalent to 0.049045 Gm. H_2SO_4.

Aromatic Sulphuric Acid.—An alcoholic solution of sulphuric acid, flavored with ginger and cinnamon, containing free sulphuric acid and ethylsulphuric acid, together equivalent to about 20 per cent. (not less than 19 per cent. nor more than 21 per cent., U. S. P.) by weight of hydrogen sulphate, H_2SO_4. It is a light-colored liquid having

a specific gravity of about 0.933 at 25° C. (77° F.). The acid should be added to the alcohol slowly in a thin stream, with constant stirring, and, when the mixture has cooled, the tincture of ginger and oil of cinnamon may be added. Upon standing, chemical action ensues and a part of the sulphuric acid is gradually converted into ethylsulphuric or sulphovinic acid, according to the equation $H_2SO_4 + C_2H_5OH = C_2H_5HSO_4 + H_2O$. The new compound, also known as acid ethyl sulphate, is soluble in water and alcohol, but is not precipitated by barium chloride; by boiling, in the presence of water, it is split up into sulphuric acid and alcohol; hence the Pharmacopœia directs in the official assay that about 10 mils. (or Cc.) of aromatic sulphuric acid, accurately weighed, shall be mixed with 60 mils. (or Cc.) of distilled water and the liquid then boiled, with the aid of a reflux condenser, for 6 hours. After cooling the liquid is diluted to 100 mils. (or Cc.) with water and titrated with normal potassium hydroxide solution, using methyl orange as indicator. As each mil. (or Cc.) of the normal alkali solution represents 0.04905 Gm. of absolute H_2SO_4, each Gm. of aromatic sulphuric acid requires not less than 3.87 nor more than 4.28 mils. (or Cc.) for neutralization, to insure conformity with the official standard.

The official assay method for aromatic sulphuric acid involves the complete decomposition, through the action of water, of any ethylsulphuric acid present into alcohol and sulphuric acid. This decomposition can be completed only when the alcohol is removed from the sphere of the chemical action as fast as it is produced. Hence even prolonged boiling in a flask fitted with an efficient reflux condenser, as directed in the Pharmacopœia will only lead to unsatisfactory results.

Complete decomposition of the ethylsulphuric acid may be brought about if the boiling be carried on in a long-necked flask, or in a flask fitted with a wide tube which serves to condense *a part* of the vapor; in this way the alcohol vapor escapes while the water vapor is condensed and returned. The same result may be obtained if the mixture of aromatic sulphuric acid and water be heated on a boiling waterbath, in a tall beaker either open or covered with a watch glass placed in such a way that there is room for the vapor to escape. Considerable saving of time has also been possible by following these methods and in a number of cases from three and a half to four hours was found sufficient in the laboratory of the Maryland State Board of Health.

The aromatic sulphuric acid of the present Pharmacopœia differs considerably from the preparation of the same name, formerly often prescribed under the name of *Elixir of Vitriol*. The latter preparation was of a brownish-red color, and very prone to precipitation; it was made by percolating 1 troy ounce of ginger and $1\frac{1}{2}$ troy ounce of cinnamon with 1 pint of alcohol, and adding the resulting tincture to a previously prepared and cooled mixture of 1 pint of alcohol and 6 troy ounces of sulphuric acid.

Diluted Sulphuric Acid.—This is made by diluting 10 parts by weight of official sulphuric acid with 84 parts of distilled water, or 50 Gms. of the former with 420 Gms. of the latter. The acid should be added gradually, with constant stirring, on account of the heat developed. It contains not less than 9.5 per cent. nor more than 10.5 per cent. of hydrogen sulphate H_2SO_4 and has a specific gravity of about 1.067 at 25° C. (77° F.).

CHAPTER XLI.

THE COMPOUNDS OF POTASSIUM.

THE Pharmacopœia recognizes 13 salts of potassium, besides 6 preparations of salts, including 3 liquids, for which working formulas are given; the following comprise the list:

Official English name.	Official Latin name.
Potassium Acetate,	Potassii Acetas.
Potassium Bicarbonate,	Potassii Bicarbonas.
Potassium Bitartrate,	Potassii Bitartras.
Potassium Bromide,	Potassii Bromidum.
Potassium Carbonate,	Potassii Carbonas.
Potassium Chlorate,	Potassii Chloras.
Potassium Citrate,	Potassii Citras.
Effervescent Potassium Citrate,	Potassii Citras Effervescens.
Potassium and Sodium Tartrate,	Potassii et Sodii Tartras.
Potassium Hydroxide,	Potassii Hydroxidum.
Potassium Hypophosphite,	Potassii Hypophosphis.
Potassium Iodide,	Potassii Iodidum.
Potassium Nitrate,	Potassii Nitras.
Potassium Permanganate,	Potassii Permanganas.
Sulphurated Potassa,	Potassa Sulphurata.
Solution of Potassium Arsenite,	Liquor Potassii Arsenitis.
Solution of Potassium Citrate,	Liquor Potassii Citratis.
Solution of Potassium Hydroxide,	Liquor Potassii Hydroxidi.
Troches of Potassium Chlorate,	Trochisci Potassii Chloratis.

Potassium Acetate. $KC_2H_3O_2$ or CH_3COOK.—This salt is prepared by neutralizing acetic acid with potassium carbonate or bicarbonate, the latter being preferable on account of its greater purity, evaporating the resulting solution to dryness, fusing the residue, and allowing the salt to solidify. The product, being very deliquescent, must be bottled while still warm, and should be well protected against air.

The salt absorbs moisture very quickly when in contact with air, which it is difficult to prevent while weighing, hence the Pharmacopœia, instead of requiring absolute purity, demands not less than 99 per cent. purity when the salt is dried to constant weight at 150° C. (302° F.).

In order to determine the quality of organic salts of potassium volumetrically, it is necessary that they first be converted into carbonate by thorough ignition, the oxygen of the atmosphere aiding in the change. In the case of potassium acetate the following reaction occurs: $2KC_2H_3O_2 + O_8 = K_2CO_3 + 3H_2O + 3CO_2$, two molecules, or 196.24 parts, of potassium acetate furnishing one molecule, or 138.2 parts of potassium carbonate. Each mil. (or Cc.) of half-normal sulphuric acid required in the official test to neutralize the carbonate

resulting from 1 Gm. of potassium acetate, represents 0.04906 Gm., or 4.906 per cent. of absolute $KC_2H_3O_2$, and hence not less than 20.19+ (practically 20.2 mils. (or Cc.)) will be required to indicate 99 per cent. purity.

Potassium Bicarbonate. $KHCO_3$.—When carbon dioxide is passed into a concentrated solution of potassium carbonate, chemical union takes place, potassium bicarbonate or acid carbonate being formed according to the equation $K_2CO_3 + H_2O + CO_2 = 2KHCO_3$. The solution is afterward decanted from any separated silica, and crystallized. Potassium bicarbonate is permanent in the air, any hygroscopic tendency indicating contamination with carbonate; this can be verified by adding to a solution of the salt barium chloride or magnesium sulphate, which are not precipitated by the pure bicarbonate. The Pharmacopœia permits slight traces of carbonate, and requires 99 per cent. purity in the salt when dried, to constant weight in a desiccator over sulphuric acid, which is determined by titration with half-normal sulphuric acid.

Potassium Bitartrate. $KHC_4H_4O_6$ or $(CHOH)_2COOHCOOK$.—Acid potassium tartrate, or cream of tartar, as it is more familiarly known, may be prepared for medicinal use by treating purified tartar with diluted hydrochloric acid for the purpose of removing the calcium present as chloride; the mixture is heated and constantly agitated while cooling. Some tartaric acid and potassium bitartrate remain finally in the mother-liquors, which are utilized in the manufacture of tartaric acid.

Crude tartar, or argol, is obtained as a natural deposit in wine casks during the fermentation of grape juice, and is purified by repeated treatment with water, clay, and animal charcoal, to remove coloring matters and other substances; the filtered solution is crystallized, the resulting product still containing 5 to 15 per cent. of calcium tartrate as an impurity, which remains.

At the present time large quantities of cream of tartar are obtained in a high state of purity and in the form of fine powder, by what is termed the precipitation method. The lees or acid residues of wine casks are partially neutralized with sodium carbonate and brought into solution in water, which solution is then allowed to percolate through soda ash contained in stone cylinders. The solution of potassium and sodium tartrate thus obtained is allowed to crystallize for the purpose of purification, after which the slightly colored crystals are redissolved in water and decomposed by addition of acetic acid, as a result of which acid potassium tartrate, almost absolutely pure, is precipitated in powder form, while sodium acetate remains in solution.

The Pharmacopœia permits the presence of not more than 0.5 per cent. of impurities and requires the absence of alum and phosphates; slight traces of lead may be present, the allowable limit being deter-

mined colorimetrically in a solution of the potassium bitartrate by comparison with an ammoniacal solution containing 0.00032 Gm. of lead nitrate in 50 mils. (or Cc.). The purity percentage is determined in a sample of the salt, previously dried to constant weight at 100° C. (212° F.), by titration with normal potassium hydroxide solution, which must show not less than 99.5 per cent. of absolute $KHC_4H_4O_6$. The equation $KHC_4H_4O_6 + KOH = K_2C_4H_4O_6 + H_2O$ shows that 1 molecule, or 188.14 Gms. of absolute potassium bitartrate requires 1 molecule, or 56.11 Gms. of potassium hydroxide for complete neutralization, and hence each mil. (or Cc.) of normal potassium hydroxide solution, containing 0.05611 Gm. of KOH, required in the official assay represents 0.18814 Gm of $KHC_4H_4O_6$.

The so-called soluble cream of tartar, or borotartrate of potassium and sodium, was formerly recognized in the German Pharmacopœia under the name *tartarus boraxatus*. It is soluble in its own weight of cold water, and is prepared by digesting 5 parts of potassium bitartrate in a solution of 2 parts of borax and 15 parts of water until dissolved; the solution is evaporated to dryness, and the residue, while still warm, reduced to powder.

Potassium Bromide. KBr.—This well known salt may be obtained by decomposing a solution of ferrous bromide with potassium carbonate, heating the mixture, filtering, evaporating the filtrate, and crystallizing. The process followed by large manufacturers is to add bromine to a solution of potassium hydroxide until the liquid remains colored, evaporate it to dryness, and expose the saline residue, mixed with charcoal, in small portions at a time, to red heat in an iron crucible; the fused mass is treated with water, the resulting solution filtered, and set aside to crystallize. When bromine and potassium hydroxide are brought together, potassium bromide and bromate are formed; thus, $6KOH + Br_6 = 5KBr + KBrO_3 + 3H_2O$; by heating the mixed salts with charcoal all bromate is reduced to bromide; thus, $KBrO_3 + C_3 = KBr + 3CO$.

The salt occurs both in cubical crystals and in granular powder, the latter variety being very convenient for dispensing purposes; it is readily soluble in water and in glycerin, but is only slightly soluble in alcohol. The Pharmacopœia demands that the salt, when dried to constant weight at 100° C. (212° F.), shall contain not less than 98.5 per cent. of absolute KBr, the most likely impurity being potassium chloride, due to the chlorine present in the bromine used in its manufacture.

The purity percentage of potassium bromide may be determined as follows: Accurately weigh about 0.4 Gm. of the salt, dried to constant weight at 100° C., dissolve it in 25 mils. (or Cc.) of distilled water in a flask and add 50 mils. (or Cc.) of tenth-normal silver nitrate solution; shake the mixture well and add 2 mils. (or Cc.) of nitric acid and 2 mils. (or Cc.) of ferric ammonium sulphate test-solution. Now

determine the excess of silver nitrate solution by running in from a burette tenth-normal potassium sulphocyanate solution until the supernatant liquid remains reddish after it is well shaken. Each mil. (or Cc.) of tenth-normal silver nitrate solution used corresponds to 0.011902 Gm. of potassium bromide or 0.007456 Gm. of potassium chloride. The difference between the number of mils. (or Cc.) of tenth-normal potassium sulphocyanate solution required and the number of mils. (or Cc.) of tenth-normal silver nitrate solution added shows the amount of the latter used up by the potassium bromide being tested, and since any potassium chloride present in the sample, owing to its lower molecular weight, will use up relatively more silver solution than potassium bromide, the exact percentage of each, provided no other substances are present which attack the silver solution, can be ascertained as follows: Calculate the number of mils (or Cc.) of tenth-normal silver solution required for the weight of salt taken, if it were absolutely pure potassium bromide and also the amount required if it were absolutely pure potassium chloride. Subtract the former from the latter and divide the remainder by 100; the result will indicate the excess of tenth-normal silver solution required to show 1 per cent. of potassium chloride. Then subtract the number of mils. (or Cc.) of silver solution necessary, as found above, for the weight of salt taken if it were pure potassium bromide from the number of mils. (or Cc.) actually used in the assay and divide the remainder by the fraction of a mil. (or Cc.) found to represent 1 per cent. of chloride; the quotient will indicate the per cent. of potassium chloride in the sample and this subtracted from 100 will express the per cent. of potassium bromide actually present in the salt. Example: 0.4 Gm. of pure potassium bromide will require 33.61 mils. (or Cc.) of tenth-normal silver solution ($0.4 \div 0.011902 = 33.608$) and 0.4 Gm. of pure potassium chloride will require 53.51 mils. (or Cc.) of the silver solution ($0.4 \div 0.007456 = 53.51$); then $53.51 - 33.61 = 19.90$ and $19.90 \div 100 = 0.199$, which shows that in the above assay process, each 0.199 mil. (or Cc.) of tenth-normal silver nitrate solution used in excess of 33.61 mils. (or Cc.) will indicate the presence of 1 per cent. of potassium chloride. Now if 16.1 mils. (or Cc.) of the sulphocyanate solution were used in the test, this would leave 33.9 mils. (or Cc.) ($50 - 6.1 = 33.9$) of silver solution as having been used up by the 0.4 Gm. of the sample taken and as 33.61 mils. (or Cc.) would be necessary if the salt were pure potassium bromide, $33.9 - 33.61 = 0.290$ mils. (or Cc.) used in excess; then $0.290 \div 0.199 = 1.457$ or practically 1.5 per cent. of chloride is shown to be present. On the other hand, if less than 33.61 mils. (or Cc.) of the silver solution is used, iodide may have been present, or some substance which does not affect the silver solution and yet has added to the weight of the salt; potassium iodide requires relatively less silver solution than potassium bromide, owing to its higher molecular weight.

Potassium Carbonate. K_2CO_3.—This compound is familiarly known as salt of tartar, a name given to it because it was at one time prepared by ignition of tartar. It is now extensively prepared from potassium chloride by a method analogous to the Leblanc process for making sodium carbonate. The purer carbonate, such as is demanded by the Pharmacopœia, is obtained by heating crystallized potassium bicarbonate to redness, whereby carbon dioxide and water are eliminated and potassium carbonate remains, the yield being about 68 or 69 per cent. The reaction is a very simple one, $2KHCO_3 = K_2CO_3 + CO_2 + H_2O$.

Potassium carbonate, on account of its very deliquescent nature, must be preserved in well stoppered bottles, in a dry place. The Pharmacopœia demands 99 per cent. of absolute K_2CO_3 for the salt when dried to constant weight at 180° C. (356° F.), and allows not more than 15 per cent. of moisture. To determine the purity percentage 1.5 Gms. of the salt previously dried as directed above, may be dissolved in 15 mils. (or Cc.) of distilled water and then titrated with normal sulphuric acid, using methyl orange solution as indicator. Since each mil. (or Cc.) of normal acid requires 0.0691 Gm. of absolute potassium carbonate for neutralization, 1.5 Gms. of the salt will require 21.49 (practically 21.5) mils. (or Cc.) to indicate not less than 99 per cent. purity.

Potassium Chlorate. $KClO_3$.—At present nearly all potassium chlorate, both in this country and in Europe, is made electrolytically, this process yielding a purer product at a lower cost. The electrolytic method was first used in Switzerland in 1891, and is most profitable in localities where ample water power is available. The process consists in passing an electric current through a heated alkaline solution of potassium chloride, whereby chlorine collects around the positive pole and potassium hydroxide around the negative pole. The solution of potassium hydroxide, by a process of circulation is carried to the compartment of the next cell containing the positive pole, and so on, by which means it comes in contact with chlorine and forms potassium chlorate, which continually crystallizes out.

Potassium chlorate may also be made by passing an excess of chlorine into a solution of potassium hydroxide, preferably at a temperature of 90° C. (194° F.). Formerly the old Liebig method was largely employed which consists in passing chlorine gas into water holding lime, or preferably magnesia, in suspension, by which means chloride and hypochlorite of the respective metals are formed. The latter salt is decomposed by heat into chlorate and chloride, and upon treating the solution with potassium chloride a reaction sets in, by which potassium chlorate and calcium or magnesium chloride are formed, the latter salts remaining in solution, while the potassium chlorate crystallizes out. Magnesia is preferred to lime, as potassium chlorate is less soluble in solution of magnesium chloride than of calcium chloride.

The reactions involved may be expressed as follows: $2Ca(OH)_2 + Cl_4 = Ca(ClO)_2 + CaCl_2 + 2H_2O$; $3Ca(ClO)_2 = Ca(ClO_3)_2 + 2CaCl_2$; $Ca(ClO_3)_2 + 2KCl = 2KClO_3 + CaCl_2$.

The salt is rarely found impure, and occurs in commerce in the form of large flat crystals, in fine powder, and in small granules. It is readily decomposed, often with explosive violence, when triturated with such substances as sugar, tannic acid, sulphur, etc. The Pharmacopœia demands not less than 99 per cent. purity, to be determined by its oxidizing effect on an acidulated solution of ferrous sulphate. Two distinct reactions occur in the official assay process: 1. $KClO_3 + 6(FeSO_4 + 7H_2O) + 3H_2SO_4 = KCl + 3Fe_2(SO_4)_3 + 45H_2O$, showing that 1 molecule, or 122.56 Gms. of potassium chlorate is capable of oxidizing 6 molecules, or 1668.132 Gms., of crystallized ferrous sulphate. 2. $2KMnO_4 + 10(FeSO_4 + 7H_2O) + 8H_2SO_4 = 5Fe_2(SO_4)_2 + K_2SO_4 + 2MnSO_4 + 8H_2O$, showing that 2 molecules of potassium permanganate, or 316.06 Gms., are necessary for the oxidation of 10 molecules, or 2780.22 Gms., of crystallized ferrous sulphate. After deducting the number of mils. (or Cc.) of tenth-normal potassium permanganate solution required for the excess of ferrous sulphate, from the number required for the parallel test with 25 mils. (or Cc.) of acidulated ferrous sulphate solution, the number of mils. (or Cc.) corresponding to the ferrous sulphate oxidized by the potassium chlorate is ascertained. Since, according to equation 2, each mil. (or Cc.) of tenth-normal potassium permanganate solution must correspond to 0.027802 Gm. of crystallized ferrous sulphate and, according to equation 1, 0.027802 Gm. of the iron salt must correspond to 0.0204266 Gm. of potassium chlorate, it follows that 1 mil. (or Cc.) of the permanganate solution also corresponds to 0.0204266 Gm. of potassium chlorate. Hence the number of mils. (or Cc.) of tenth-normal potassium permanganate solution ascertained, as above stated, to correspond to the ferrous sulphate oxidized by the potassium chlorate, when multiplied by 2.04266 (0.0204266 × 100) and divided by the weight of the sample originally taken, will express the percentage of pure potassium chlorate present.

Potassium Citrate. $K_3C_6H_5O_7 + H_2O$ or $C_3H_4OH(COOK)_3$. H_2O.— This salt is prepared by neutralizing a solution of citric acid with potassium carbonate or bicarbonate, and evaporating the solution to dryness, with constant stirring, so as to obtain the salt in small granules. The finished product retains a little over $5\frac{1}{2}$ per cent. of water, which it loses entirely when heated to 200° C. (392° F.), but should be free from impurities; the commercial article is frequently acid, showing imperfect saturation. As the salt is deliquescent in moist air it must be well protected.

The Pharmacopœia requires that potassium citrate, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 99 per cent. of hydrated or crystallized salt, and directs

that this be determined by thoroughly carbonizing about 1 Gm. of the salt, previously dried as stated above, boiling the residue with an excess of half-normal sulphuric acid and determining the excess of acid by titration with half-normal potassium hydroxide solution. Citric acid being tribasic, 2 molecules, or 648.72 parts, of potassium citrate will yield 3 molecules, or 414.6 parts, of carbonate; thus, $2K_3C_6H_5O_7.H_2O + O_{18} = 3K_2CO_3 + 9CO_2 + 7H_2O$; hence each mil. (or Cc.) of half-normal acid, which requires 0.03455 Gm. of potassium carbonate for neutralization, must correspond to 0.05406 Gm. of hydrated or crystallized potassium citrate, for 414.6 : 648.72 : : 0.03455 : 0.05406.

Effervescent Potassium Citrate.—This preparation contains about 20 per cent. of potassium citrate and has already been considered on page 476 in the chapter on Granular Effervescent Salts.

Potassium and Sodium Tartrate. $KNaC_4H_4O_6 + 4H_2O$ or $(CHOH)_2COONaCOOK + 4H_2O$.—This salt is commercially known as Rochelle Salt from the fact that it was first obtained at Rochelle, France, by an apothecary named Seignette, more than two hundred years ago. It is prepared by neutralizing the free acid in cream of tartar with sodium carbonate, whereby a normal double tartrate is produced; the solution, which must be neutral, is boiled for a short time, filtered, concentrated, and set aside to crystallize, the crystals being afterward pulverized. According to the following equation, $2KHC_4H_4O_6 + (Na_2CO_3 + 10H_2O) = 2(KNaC_4H_4O_6.4H_2O) + CO_2 + 3H_2O$, 8 parts of official cream of tartar will require about 6 parts of crystallized pure sodium carbonate, yielding about 12 parts of crystallized Rochelle Salt.

Potassium and sodium tartrate is recognized in the British Pharmacopœia by the name of *soda tartarata*, and in the German Pharmacopœia as *tartarus natronatus;* it is also known as *sal Seignetti*.

The Pharmacopœia requires that the salt shall contain not less than 73.71 per cent. nor more than 77.39 per cent. of anhydrous potassium and sodium tartrate, corresponding to not less than 99 per cent. of the hydrated or crystallized salt. The purity percentage is determined by thoroughly carbonizing about 2 Gms. of the salt, boiling the residue with an excess of half-normal sulphuric acid and titrating the excess of acid by means of half-normal potassium hydroxide solution. The equation $KNaC_4H_4O_6 + 4H_2O + O_5 = KNaCO_3 + 3CO_2 + 6H_2O$ shows that 1 molecule or 282.2 Gms. of crystallized potassium and sodium tartrate will yield 1 molecule or 122.1 Gms. of the double carbonate; the latter is capable of neutralizing 98.086 Gms. of absolute sulphuric acid or 2000 mils. (or Cc.) of half-normal sulphuric acid. Since each mil. (or Cc.) of the half-normal acid requires 0.030525 Gm. of the double carbonate for complete neutralization, it must correspond to 0.07055 Gm. of the crystallized or hydrated potassium and sodium tartrate or 0.052533 Gm. of the anhydrous salt. Each Gm. of crystallized potassium and sodium tartrate, yielding 0.7446 +

Gm. of anhydrous salt and when ignited 0.43267 Gm. of the double carbonate, must, after thorough carbonization, neutralize not less than 14.03+ mils. (or Cc.) nor more than 14.73 mils. (or Cc.) of half-normal acid to meet the pharmacopœial requirements.

Potassium Hydroxide. KOH.—This compound, better known as *caustic potash*, is obtained by decomposing a solution of potassium carbonate with milk of lime, evaporating the clear filtrate in perfectly clean iron or silver vessels until a small quantity of the liquid congeals upon cooling, and then pouring it into cylindrical moulds, whence the sticks are removed while still warm.

The purity of the product obtained depends upon the quality of the potassium carbonate employed, and if made from the bicarbonate it is of much better quality. White caustic potash in sticks, labelled *potassa by lime*, is the kind generally used for pharmaceutical purposes, and should contain not over 5 or 6 per cent. of moisture; commercial caustic potash is sometimes found to contain as much as 15 or 20 per cent. of water. For chemical purposes potassium hydroxide is purified by means of alcohol or baryta, being then known as *potassa by alcohol* or *potassa by baryta*. The purest potassium hydroxide is obtained by adding pure metallic potassium in small pieces to distilled water in a silver dish and evaporating the solution.

Potassium hydroxide is a powerful caustic, very deliquescent, and rapidly absorbs carbon dioxide and moisture from the air; it must therefore be handled carefully and preserved in tightly stoppered bottles. It is soluble in less than its own weight of water and in about twice its weight of alcohol at 25° C. (79° F.).

The Pharmacopœia requires that official potassium hydroxide shall contain not less than 85 per cent. of absolute KOH, which is determined by titrating a solution of potassium hydroxide with normal hydrochloric acid; the solution is made with distilled water previously boiled and cooled, and then treated with a solution of barium chloride for the purpose of removing any carbonate present, the clear filtrate only being titrated. As each mil. (or Cc.) of normal hydrochloric acid will neutralize 0.05611 Gm. of pure KOH, the number of mils. (or Cc.) of normal acid required in the official assay, when multiplied by 5.611 (0.05611 × 100) and divided by the weight of potassium hydroxide taken, will express the percentage of absolute KOH present.

Potassium Hypophosphite. KH_2PO_2.—Although this salt can be made by boiling phosphorus with solution of potassium hydroxide, it is preferably obtained by adding potassium carbonate to a solution of calcium hypophosphite, when calcium carbonate will be precipitated and potassium hypophosphite remain in solution, which can be recovered by filtering the mixture and carefully evaporating the filtrate on a waterbath, with constant stirring, until a granular salt results. The

following equation shows the decomposition: $Ca(H_2PO_2)_2 + K_2CO_3 = 2KH_2PO_2 + CaCO_3$.

Potassium hypophosphite is very deliquescent, and must be preserved in tightly stoppered bottles; as it readily explodes when intimately mixed with oxidizing agents, trituration with such substances must be avoided.

The official salt is required to contain, when dried to constant weight in a desiccator over sulphuric acid, not less than 98 per cent. of absolute KH_2P_2O, which is directed to be determined volumetrically after conversion into phosphate by treatment with nitric acid. The method is practically identical with that explained under Phosphoric Acid on page 562, trisilver phosphate being formed by addition of tenth-normal silver nitrate solution to a solution of the newly formed phosphate. Absolutely accurate results can be obtained in the official process of assay only if phosphite and phosphate are absent in the original salt. Gravimetric determination as magnesium pyrophosphate after removal of any phosphite and phosphate present by means of lead acetate and subsequent oxidation of the hypophosphite to phosphate by means of bromine, as first recommended by Jowett, gives accurate results and is no more laborious than the official volumetric method.

Potassium Iodide. KI.—When iodine is added to a solution of potassium hydroxide the two substances combine, forming potassium iodide and iodate; thus, $6KOH + I_6 = 5KI + KIO_3 + 3H_2O$. The process of manufacturing this salt is analogous to that given for potassium bromide, the iodate being subsequently reduced to iodide by heating with charcoal.

Potassium iodide occurs in commerce both in transparent and opaque cubical crystals, and as a white granular powder is very convenient for dispensing purposes; the opaque crystals are the result of crystallization from an alkaline solution. The limit of alkali allowed by the Pharmacopœia in the salt is determined by adding 0.1 mil. (or Cc.) of tenth-normal sulphuric acid to a solution of 1 Gm. of potassium iodide in 10 mils. (or Cc.) of distilled water, when the subsequent addition of 1 drop of phenolphthalein solution should not cause any color. The official test for the presence of potassium cyanide, due to cyanogen derived from the iodine, involves the formation of potassium ferrocyanide, which, reacting with ferrous sulphate, rapidly produces a blue color, owing to the oxidizing effect of the air.

The Pharmacopœia requires that when dried to constant weight at 100° C. (212° F.) the salt shall contain not less than 99 per cent. of absolute KI, to be determined by titration with tenth-normal silver nitrate solution, after the manner explained under Potassium Bromide, each mil. (or Cc.) of the silver solution required for complete precipitation corresponding to 0.016602 Gm. of pure KI. Any excess of tenth-normal silver nitrate solution required in the assay, over and

above the calculated theoretical quantity, may be due to the presence of bromide or chloride, both of which have a lower molecular weight than potassium iodide.

Potassium Nitrate. KNO_3.—The sources of this salt were at one time chiefly the natural deposits in India and extensive plantations in Europe and elsewhere for the artificial production of potassium nitrate by putrefaction of animal and vegetable matter in the presence of wood-ashes and calcareous earth. It is now largely obtained by mutual decomposition of potassium chloride and native sodium nitrate, advantage being taken of the lesser solubility of the newly formed sodium chloride in hot water to rid the solution of this impurity upon concentration by boiling. The potassium nitrate subsequently crystallizes out, and is further purified by re-solution and re-crystallization.

Potassium nitrate is to be had both in the form of large crystals and as a fine granular powder; the latter is preferred for pharmaceutical purposes, and is largely obtained from manufacturers of gunpowder, who require a pure article for their purposes.

The Pharmacopœia requires that the salt, when dried to constant weight at 100° C. (212° F.), shall contain not less than 99 per cent. of pure KNO_3, which is determined by first converting the nitrate into chloride by evaporating a solution of the salt in hydrochloric acid to dryness and repeating the operation. After solution of the potassium chloride thus obtained, it is titrated with tenth-normal silver nitrate solution, and from the quantity of silver nitrate solution required is subtracted the quantity which would be consumed by the chlorides present in an equivalent weight of the salt originall taken, and previously determined in about 1 Gm. of the salt accurately weighed. As each molecule of potassium nitrate, or 101.11 Gms., will yield 1 molecule, or 74.56 Gms. of potassium chloride, each mil. (or Cc.) of tenth-normal silver nitrate solution consumed in the official assay, and corresponding to 0.007456 Gm. of potassium chloride, will represent 0.010111 Gm. of pure KNO_3.

The name saltpetre, or nitre, is used almost exclusively in commerce for this salt, which when fused and cast into round moulds is sold under the name *sal prunelle*.

Potassium Permanganate. $KMnO_4$.—In the manufacture of this compound the first step necessary is the production of potassium manganate, by heating to semi-fusion at a dull-red heat, an intimate mixture of manganese dioxide, potassium hydroxide, and potassium chlorate, when the following reaction occurs: $3MnO_2 + 6KOH + KClO_3 = 3K_2MnO_4 + KCl + 3H_2O$. The green fused mass is then treated twice with boiling water, whereby the potassium manganate is converted into permanganate—$3K_2MnO_4 + 2H_2O = 2KMnO_4 + MnO_2 + 4KOH$—manganese dioxide being again precipitated and

potassium hydroxide remaining in solution with the permanganate. The presence of potassium hydroxide in the liquid prevents a full yield of permanganate by holding a portion of the manganate in solution without change; a stream of carbon dioxide is therefore passed into the liquid to neutralize the alkali and thus allow all the manganate to be converted into permanganate and dioxide; in place of carbon dioxide a current of chlorine or ozone is often used, and the addition of sulphuric acid has also been found very effective. Finally, after decantation and filtration through asbestos, the solution is concentrated and set aside to crystallize. As potassium permanganate is readily decomposed by organic matter, all dust and dirt must be excluded during the last steps of the process.

The official method of valuation of potassium permanganate by means of oxalic acid depends upon the ready deoxidation of the salt by all reducing substances, five atoms of oxygen being liberated from every two molecules of the permanganate. In the official test the oxalic acid is completely converted by oxidation into carbon dioxide and water, as shown by the following equation: $5(H_2C_2O_4 + 2H_2O) + 2KMnO_4 + 3H_2SO_4 = 10CO_2 + K_2SO_4 + 2MnSO_4 + 18H_2O$, 630.24 parts of crystallized oxalic acid requiring 316.06 parts of pure permanganate. The Pharmacopœia requires potassium permanganate to be of 99 per cent. purity, when dried to constant weight in a desiccator over sulphuric acid, and as each mil. (or Cc.) of tenth-normal oxalic acid solution, containing 0.0063024 Gm. of the acid, requires 0.0031606 Gm. of pure $KMnO_4$ for complete oxidation, the number of mils. (or Cc.) of the oxalic acid solution consumed, when multiplied by 0.31606 (0.0031606×100) and divided by the weight of potassium permanganate taken for the assay, will express the percentage of pure $KMnO_4$ present in the sample.

Since potassium permanganate is easily decomposed, it should never be triturated or dispensed with readily oxidizable or organic substances. Stains produced by the salt in a mortar or on the hands are best removed with oxalic acid solution, either alone or with little sulphuric acid.

While potassium permanganate is used to some extent in medicine, it is of special interest to pharmacists as an oxidizing agent in volumetric analysis.

Solution of Potassium Arsenite.—This preparation can be more conveniently studied in connection with the preparations of arsenic.

Solution of Potassium Citrate.—The Pharmacopœia very properly directs the extemporaneous preparation of this solution, as it does not keep well and soon loses its refreshing taste. The proportions of citric acid, 6 Gms., and potassium bicarbonate, 8 Gms., in the official formula show a slight excess of citric acid over the quantity necessary to form a neutral salt, which improves the flavor of the

finished product. The solution contains about 8.55 Gms. of potassium citrate and 0.43 Gm. of citric acid in 100 mils. (or Cc.) besides some carbonic acid, which corresponds to about 38 grains of the salt in each fluidounce.

The Pharmacopœia requires that the solution shall contain not less than 8 per cent. of anhydrous potassium citrate, to be determined by evaporating to dryness about 15 Gms. of the solution, accurately weighed, and treating the residue, as in the case of potassium citrate by carbonizing and then titrating with half-normal sulphuric acid.

Although the name *mistura potassii citratis* is sometimes applied to this solution, the latter differs from the preparation formerly recognized by that name and more familiarly known as *neutral mixture*. The former preparation was made by neutralizing fresh lemon juice, strained through cotton, with potassium bicarbonate, and possessed, therefore, a more agreeable flavor, although of uncertain strength. Some physicians still prefer the old *neutral mixture* to the present official solution in many cases.

Solution of Potassium Hydroxide.—The official Liquor Potassii Hydroxidi can be made either by decomposition of a solution of pure potassium carbonate, obtained by heating the bicarbonate, with milk of lime or by simple solution of 60 Gms. of potassium hydroxide in 940 Gms. of distilled water, the latter being generally preferred by pharmacists as a matter of convenience, while the former is followed by manufacturing chemists for economical reasons. If simple solution of the potassium hydroxide be employed, it is important that the percentage of KOH present be known, in order to insure a 5 per cent. solution; the above proportions are calculated for 85 per cent. potassium hydroxide, and the proper quantity of a higher or lower grade can be readily found by dividing 5100 by the percentage of potassium hydroxide contained in the sample. This is arrived at as follows: the official 5 per cent. solution requires 50 Gms. of absolute or 100 per cent. KOH for 1000 Gms. of finished product, but a larger quantity of a poorer sample or a smaller quantity of a richer sample than the official potassium hydroxide will be required. In other words, the quantity of potassium hydroxide necessary will be in inverse proportion to the percentage of KOH present. Knowing that 60 Gms. of 85 per cent. potassium hydroxide are required, and representing the unknown percentage strength by p and the unknown quantity by x, we may say $p\% : 85\% :: 60 : x$, from which we derive $x = \frac{85 \times 60}{p}$, or $\frac{5100}{p}$. Thus, if the potassium hydroxide contains only 80 per cent. of KOH, it will require 63.75 (5100 ÷ 80) Gms. of potassium hydroxide and 936.25 Gms. of distilled water, for 63.75 at 80 per cent. is equal to 60 at 85 per cent., 51 being the result in both cases and yielding practically 1000 Gms. of a 5 per cent. solution. On the other hand, if the potassium hydroxide to be used contains 88 per cent. of pure KOH, it will

require only 57.95 Gms. of the potassium hydroxide and 942.05 Gms. of distilled water to make 1000 Gms. of the official solution, for 57.95 at 88 per cent. is equal to 60 at 85 per cent.

In order to preserve the quality of the solution of potassium hydroxide it is essential that it be kept in securely stoppered bottles, to avoid absorption of carbon dioxide; the bottles should be made of green glass, as flintware is easily acted upon, and the stoppers should be thinly coated with paraffin or petrolatum, to prevent their becoming "fixed." Solution of potassium hydroxide should never be filtered through paper, which is rapidly attacked by the alkali; large volumes are best decanted or siphoned from any sediment, while small quantities may be conveniently filtered through glass-wool or asbestos.

The official solution of potassium hydroxide has a specific gravity of about 1.046 at 25° C. (77° F.), and should contain not less than 4.5 per cent. of pure KOH, which is determined by titrating a definite weight of the solution, after removal of any carbonate present by means of barium chloride solution, with normal hydrochloric acid, each mil. (or Cc.) of which consumed corresponds to 0.05611 Gm. of pure potassium hydroxide.

Sulphurated Potassa.—This product is not a true chemical compound, and is recognized in the Pharmacopœia as a mixture composed of potassium polysulphides and potassium thiosulphate. Commercially it is often designated as liver of sulphur. It is obtained by gradually heating a mixture of sulphur and potassium carbonate in a crucible until effervescence ceases and then increasing the heat to dull redness to produce perfect fusion; the contents of the crucible are poured out on a stone slab, covered to prevent access of air, and allowed to solidify. The reaction results in the escape of carbon dioxide and the formation of potassium sulphides and potassium thiosulphate, as shown by the equation $3K_2CO_3 + 4S_2 = 2K_2S_3 + K_2S_2O_3 + 3CO_2$; more or less potassium sulphate may also be formed if the temperature be not properly controlled, by decomposition of the thiosulphate, thus $4K_2S_2O_3 = 3K_2SO_4 + K_2S_5$.

When freshly prepared, sulphurated potassa has a liver-brown color, which gradually changes, especially when exposed to air, by absorption of moisture, oxygen and carbon dioxide, to greenish-yellow, and finally to gray. It should be preserved in tightly stoppered bottles. Sulphurated potassa is very soluble in water, but if treated with alcohol only the sulphides present are dissolved. The Pharmacopœia requires that the compound shall contain an amount of sulphides corresponding to not less than 12.8 per cent. of sulphur, to be determined by adding a solution of 1 Gm. of crystallized copper sulphate in 15 mils. (or Cc.) of distilled water to a solution of 1 Gm. of sulphurated potassa in 10 mils. (or Cc.) of distilled water; the filtrate from this mixture, after acidulation with acetic acid, should not yield a

black precipitate upon addition of hydrogen sulphide solution. Two molecules of crystallized copper sulphate, or 499.44 Gms., require 2 atoms of sulphur, or 64.14 Gms., present as sulphides, for complete precipitation of the copper, and 1 Gm. will therefore require 0.1284 + Gm., which is equivalent to 12.84 + per cent. of the 1 Gm. of sulphurated potassa used in the assay.

Besides the official potassium salts, a few not recognized in the Pharmacopœia are occasionally prescribed by physicians, such as potassium benzoate, potassium salicylate, potassium tartrate, etc., which can be easily prepared extemporaneously, after calculating the necessary quantity of potassium bicarbonate and of the respective acid to make the required quantitiy of the salt wanted, thus: 100 Gms. or grains, of potassium benzoate will require 47 Gms., or grains of potassium bicarbonate and 57 Gms., or grains, of benzoic acid, etc.

CHAPTER XLII.

THE COMPOUNDS OF SODIUM.

THE official salts of sodium resemble those of potassium in many respects and are frequently prepared by analogous processes. Twenty-seven salts, besides 5 liquid and 2 solid preparations, are recognized in the Pharmacopœia, as follows:

Official English Name.	Official Latin Name.
Sodium Acetate,	Sodii Acetas.
Sodium Arsenate,	Sodii Arsenas.
Exsiccated Sodium Arsenate,	Sodii Arsenas Exsiccatus.
Sodium Benzoate,	Sodii Benzoas.
Sodium Benzosulphinide,	Sodii Benzosulphinidum.
Sodium Bicarbonate,	Sodii Bicarbonas.
Sodium Borate,	Sodii Boras.
Sodium Bromide,	Sodii Bromidum.
Sodium Cacodylate,	Sodii Cacodylas.
Sodium Carbonate, Monohydrated,	Sodii Carbonas Monohydratus.
Sodium Chloride,	Sodii Chloridum.
Sodium Citrate,	Sodii Citras.
Sodium Cyanide,	Sodii Cyanidum.
Sodium Glycerophosphate,	Sodii Glycerophosphas.
Sodium Hydroxide,	Sodii Hydroxidum.
Sodium Hypophosphite,	Sodii Hypophosphis.
Sodium Indigotindisulphonate,	Sodii Indigotindisulphonas.
Sodium Iodide,	Sodii Iodidum.
Sodium Nitrite,	Sodii Nitris.
Sodium Perborate,	Sodii Perboras.
Sodium Phenolsulphonate,	Sodii Phenolsulphonas.
Sodium Phosphate,	Sodii Phosphas.
Effervescent Sodium Phosphate,	Sodii Phosphas Effervescens.
Exsiccated Sodium Phosphate,	Sodii Phosphas Exsiccatus.
Sodium Salicylate,	Sodii Salicylas.
Sodium Sulphate,	Sodii Sulphas.
Exsiccated Sodium Sulphite,	Sodii Sulphis Exsiccatus.
Sodium Thiosulphate,	Sodii Thiosulphas.
Solution of Chlorinated Soda,	Liquor Sodæ Chlorinatæ.
Physiological Solution of Sodium Chloride,	Liquor Sodii Chloridi Physiologicus.
Solution of Sodium Arsenate,	Liquor Sodii Arsenatis.
Solution of Sodium Glycerophosphate,	Liquor Sodii Glycerophosphatis.
Solution of Sodium Hydroxide,	Liquor Sodii Hydroxidi.
Troches of Sodium Bicarbonate,	Trochisci Sodii Bicarbonatis.

Sodium Acetate. $NaC_2H_3O_2 + 3H_3O$ or $CH_3COONa.3H_2O$.—This salt may be prepared by neutralizing acetic acid with sodium carbonate or bicarbonate, concentrating the resulting solution and crystallizing; in a crude form it is extensively obtained in the manufacture of acetic acid, and may be purified by roasting and other

processes. Sodium acetate differs from potassium acetate in containing nearly 40 per cent. of water of crystallization, and in its stability upon exposure to air; hence less care is necessary in its preservation; it is about one-third as soluble in water and far less soluble in alcohol than the potassium salt.

The valuation of the so-called organic sodium salts is performed, as in the case of the corresponding potassium salts, by conversion into carbonate by ignition and subsequent titration with half-normal acid. The following equation, $2(NaC_2H_3O + 3H_2O) + O_8 = Na_2CO_3 + 3CO_2 + 9H_2O$, shows that two molecules, or 272.14 parts, of crystallized sodium acetate yield, upon complete ignition, one molecule, or 106 parts, of anhydrous sodium carbonate; hence each mil. (or Cc.) of half-normal sulphuric acid, requiring 0.0265 Gm. of sodium carbonate for neutralization, corresponds to 0.04101 Gm. of anhydrous or 0.068035 Gm. of crystallized sodium acetate. The Pharmacopœia demands that the official sodium acetate shall be not less than 99.5 per cent. pure, and contain not less than 59.97 per cent., nor more than 62.96 per cent. of pure anhydrous $NaC_2H_3O_2$. One Gm. of the crystallized salt, after complete carbonization, will therefore require not less than 14.62 mils. (or Cc.) nor more than 15.35 mils. (or Cc.) of half-normal acid to fulfill the pharmacopœial requirement.

Sodium Arsenate. $Na_2HAsO_4 + 7H_2O$.—The official salt, as shown by the chemical formula, is disodium orthoarsenate, and bears a close analogy to the official sodium phosphate; the exact composition must depend upon the proportions of the ingredients used in its manufacture. Sodium arsenate is usually obtained by fusing together, at a red heat, arsenic trioxide, anhydrous sodium carbonate, and sodium nitrate; effervescence ensues, and, when complete, quiet fusion has set in, the residue will consist of sodium pyroarsenate, as shown by the following equation: $As_2O_3 + 2NaNO_3 + NaC_2O_3 = Na_4As_2O_7 + N_2O_3 + CO_2$. The fused mass, having been poured on a stone slab and allowed to solidify, is dissolved, while still warm, in water, whereby the sodium pyroarsenate is converted into orthoarsenate by the appropriation of water; thus, $Na_4As_2O_7 + H_2O = 2Na_2HAsO_4$. The solution is set aside to crystallize, when a salt containing 40.4 per cent. of water, and having the above formula, will be obtained.

In the British Pharmacopœia the title Sodii Arsenas is applied to the anhydrous salt, described below.

The official salt, upon exposure to dry air, gradually loses a portion of its water of crystallization until a salt of the composition $Na_2HAsO_4 + 2H_2O$ remains, containing only 16.2 per cent. of water; hence, it should be preserved in tightly stoppered bottles.

The Pharmacopœia requires that the official sodium arsenate shall be 99 per cent. pure and contain not less than 58.98 per cent., nor more than 61.92 per cent. of anhydrous disodium hydrogen arsenate, which is determined by heating a solution of the salt to 80° C. (176° F.)

and adding hydrochloric acid and potassium iodide; after 15 minutes the liquid is cooled and the liberated iodine titrated with tenth-normal sodium thiosulphate solution. The reaction occurring in the acid liquid involves the formation of arsenic and hydriodic acids, which immediately decompose each other, liberating iodine and water, and forming arsenous acid as shown by the equations $Na_2HAsO_4 + 4HCl + 2KI = H_3AsO_4 + 2HI + 2NaCl + 2KCl$ and $H_3AsO_4 + 2HI = H_3AsO_3 + I_2 + H_2O$. It is thus seen that 2 atoms, or 253.84 Gms., of iodine will be liberated for every molecule, or 185.97 Gms., of anhydrous sodium arsenate present, and hence each mil. (or Cc.) of tenth-normal sodium thiosulphate solution required by the liberated iodine, and corresponding to 0.012692 Gm. of iodine, must also correspond to 0.009298 Gm. of anhydrous sodium arsenate. The number of mils. (or Cc.) of tenth-normal sodium thiosulphate solution required in the official assay, when multiplied by 0.9298 (0.009298 × 100) and divided by the weight of sodium arsenate taken, will express the percentage of anhydrous sodium arsenate present in the sample.

Exsiccated Sodium Arsenate. Na_2HAsO_4.—This salt, also known as anhydrous sodium arsenate, is prepared by allowing the crystallized salt to effloresce at a temperature between 40° and 50° C. (104° and 122° F.) until completely disintegrated; the temperature is then gradually increased to 150° C. (302° F.) and continued until the product ceases to lose weight. It is then reduced to a fine powder. The object of first allowing the crystals to effloresce at a moderate temperature is to prevent fusion of the salt in its own water of crystallization, as the latter would be much more difficult to drive off in that condition. Each Gm. of the exsiccated salt corresponds to 1.678 + Gm. of the crystallized salt, but in all other respects the two salts are identical.

The Pharmacopœia requires that exsiccated sodium arsenate, when dried to constant weight at 150° C. (302° F.), shall contain not less than 98 per cent. of pure anhydrous disodium hydrogen arsenate, which is determined in the same manner as directed for the assay of the crystallized sodium arsenate.

The reason for directing the use of exsiccated sodium arsenate in pharmacopœial preparations is to insure uniformity in the arsenic content, since the crystallized sodium arsenate may contain variable proportions of water, depending upon the temperature at which the crystals have been formed and the care with which they have been preserved.

Sodium Benzoate. $NaC_7H_5O_2$ or C_6H_5COONa.—This salt may be conveniently prepared by suspending benzoic acid in hot water and slowly adding sufficient sodium bicarbonate to form a neutral solution, which is then filtered and evaporated, with frequent stirring, on a waterbath, to dryness. 100 parts of benzoic acid require about 70

parts of official sodium bicarbonate and yield about 118 parts of sodium benzoate. The salt can also be obtained in crystalline form, having the composition $NaC_7H_5O_2 + H_2O$; but, as it effloresces readily, the Pharmacopœia has recognized only the anhydrous salt.

The Pharmacopœia requires that sodium benzoate, when dried to constant weight at 110° C. (230° F.), shall contain not less than 99 per cent. of pure $NaC_7H_5O_2$, which is determined in the same manner as directed for the assay of sodium acetate, by ignition of the salt and titration of the alkaline residue with half-normal acid. The equation $2NaC_7H_5O_2 + O_{30} = Na_2CO_3 + 13CO_2 + 5H_2O$ shows that 2 molecules, or 288.08 Gms., of sodium benzoate will yield 1 molecule, or 106 Gms., of sodium carbonate, which latter is capable of neutralizing 98.086 Gms. of absolute sulphuric acid; hence each mil. (or Cc.) of half-normal sulphuric acid, containing 0.0245215 Gm. of absolute sulphuric acid, consumed by the alkaline residue left upon ignition in the official assay must correspond to 0.07202 Gm. of pure sodium benzoate.

Sodium Benzosulphinide. $NaC_7H_4O_3NS + 2H_2O$.—This compound, also known as sodium saccharin and crystallose, may be prepared by neutralizing an aqueous solution of sodium carbonate or sodium bicarbonate with benzosulphinide, and then allowing the solution to crystallize slowly.

While benzosulphinide (saccharin) requires nearly 300 times its weight of water for solution at 25° C. (77° F.), its sodium salt is soluble in 1.2 times its weight of water, and is therefore preferred for many purposes. It is sometimes wrongly called soluble saccharin, and its only use in pharmacy and medicine is as a convenient sweetening agent when the use of sugar is contra-indicated by disease.

Sodium Bicarbonate. $NaHCO_3$.—This well known compound is manufactured on a large scale by different processes. If sodium carbonate in crystalline form be treated with carbon dioxide, anhydrous sodium bicarbonate, or acid carbonate, will be formed and water eliminated; thus, $(Na_2CO_3 + 10H_2O) + CO_2 = 2NaHCO_3 + 9H_2O$; by using a mixture of anhydrous and crystallized sodium carbonate, a part of the eliminated water will be required for converting the former into bicarbonate, the rest being allowed to escape by drainage. Sodium bicarbonate is obtained also as an intermediate product in the manufacture of the normal carbonate by the Solvay ammonia-soda process, wherein a concentrated solution of sodium chloride is mixed with ammonia and then saturated with carbon dioxide under pressure. Sodium bicarbonate is precipitated and ammonium chloride remains in solution. In either case the newly formed sodium bicarbonate is washed with small quantities of water for the purpose of removing the more soluble impurities.

The product of the Solvay process requires careful purification,

owing to contamination with ammonium salts, especially ammonium carbonate; hence sodium bicarbonate, prepared from normal carbonate, is preferred for medicinal purposes.

Sodium bicarbonate is also made by passing carbon dioxide into a saturated solution of sodium carbonate, when the much less soluble bicarbonate is precipitated. Large quantities of sodium bicarbonate are produced at Natrona, Pa., and near Syracuse, N. Y.

Commercial sodium bicarbonate is sometimes contaminated with carbonate and chloride; but if a pure salt is wanted, this may be readily obtained by percolating the commercial article with cold distilled water and drying the purified residue with moderate heat only.

The Pharmacopœia requires that sodium bicarbonate, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 99 per cent. of pure $NaHCO_2$, which is determined by titrating a solution of the dried salt, made with cold distilled water, with normal sulphuric acid; each mil. (or Cc.) of the normal acid consumed corresponds to 0.08401 Gm. of pure sodium bicarbonate, or 1 Gm. of the official salt will neutralize at least 11.78 mils. (or Cc.) of normal acid.

Sodium Borate. $Na_2B_4O_7 + 10H_2O$.—The more familiar name borax is usually applied to this compound, which, although sometimes wrongly called sodium biborate, is, as shown by the chemical formula, sodium tetraborate or pyroborate. It is found extensively in different parts of the world, particularly in California, where immense quantities are obtained from the blue mud of certain lakes. Solution and recrystallization are resorted to for the purpose of purification. Considerable quantities of borax are obtained also from crude boric acid, by treating it with sodium carbonate, and from various minerals containing borates of sodium, calcium, and magnesium.

Since 1910 considerable quantities of borax are made by heating a mixture of native borates, such as the minerals colemanite, $Ca_2B_6O_{11} + 11H_3O$, borocalcite, CaB_4O_7 etc., and sodium sulphate to redness, but not to fusion in suitable rotary furnaces, when the following reactions occur: $2Ca_2B_6O_{11} + 3Na_2SO_4 = 3Na_2B_4O_7 + 3CaSO_4 + CaO$ and $CaB_4O_7 + Na_2SO_4 = Na_2B_4O_7 + CaSO_4$; after cooling the borax is dissolved in water and allowed to crystallize.

The Pharmacopœia requires that borax shall contain not less than 52.32 per cent. nor more than 54.92 per cent. of pure anhydrous sodium borate, corresponding to not less than 99 per cent. of the crystallized salt, which is determined by titrating a solution of sodium borate with normal hydrochloric acid, using methyl orange as indicator. The reaction occurring results in the formation of sodium chloride and the liberation of boric acid, which latter is indifferent to methyl orange; hence as soon as all sodium borate has been decomposed, the slightest excess of hydrochloric acid will produce the characteristic

red color with the indicator. The equation ($Na_2B_4O_7 + 10H_2O$) + $2HCl = 2NaCl + 4H_3BO_3 + 5H_2O$ shows that 1 molecule, or 382.16 Gms., of pure crystallized sodium borate, equivalent to 1 molecule, or 201.36 Gms., of the anhydrous salt, requires 2 molecules, or 72.936 Gms., of hydrogen chloride (absolute hydrochloric acid) for complete decomposition, and therefore each mil. (or Cc.) of normal hydrochloric acid, containing 0.036468 Gm. of absolute acid, must correspond to 0.1010 Gm. of pure anhydrous sodium borate. One Gm. of official sodiun borate will require not less than 5.18 mils. (or Cc.) nor more than 5.44 mils. (or Cc.) of normal hydrochloric acid to fulfill the pharmacopœial requirements.

Borax is of special interest in pharmacy on account of its peculiar behavior with other substances. It is incompatible with mucilage of acacia, causing gelatinization, which can, however, be prevented by the presence of sugar; it precipitates many alkaloids from their solution, such as cocaine, morphine, atropine, quinine, etc., except in the presence of glycerin; it forms a damp, almost moist, mixture when triturated with alum; in the presence of glycerin it decomposes alkali bicarbonates with effervescence; and, lastly, while an aqueous solution of borax shows an alkaline reaction toward litmus, a solution in glycerin has a decided acid reaction, which is changed to alkaline upon large dilution with water. This last behavior is also observed with other bodies resembling glycerin, such as mannitol, glucose, etc.

Sodium Bromide. NaBr.—This salt is prepared in a manner similar to potassium bromide, either by decomposing a solution of ferrous bromide with sodium carbonate or by treating a solution of sodium hydroxide with bromine and finally reducing with charcoal any sodium bromate formed.

Sodium bromide is somewhat hygroscopic, but does not deliquesce upon exposure to the air. As in the case of the corresponding potassium salt, some chloride is usually present.

The Pharmacopœia requires that the salt, when dried to constant weight at 100° C. (212° F.), shall contain not less than 98.5 per cent. of pure sodium bromide, which is determined exactly in the same manner as directed for the assay of potassium bromide, except that a different factor must be used for the calculation, since each mil. (or Cc.) of the tenth-normal silver nitrate solution consumed corresponds to 0.010292 Gm. of pure NaBr.

Sodium Cacodylate. $Na(CH_3)_2ASO_2$.—The name sodium dimethylarsenate indicates more clearly the chemical composition of this salt, which crystallizes with variable proportions of water. It is made by distilling arsenic trioxide with potassium acetate, when the following reaction occurs: $As_2O_3 + 4CH_3COOK = As_2(CH_3)_4O + 2K_2CO_3 + 2CO_2$; the distillate, consisting chiefly of cacodylic oxide, mentioned in the reaction, and some cacodyl, $As_2(CH_3)_4$ (so named on account

of the disgusting odor of the compounds), is oxidized with mercuric oxide, forming cacodylic acid, $H(CH_3)_2AsO_2$, which is then neutralized with sodium hydroxide, the solution being finally concentrated and allowed to crystallize, or evaporated to dryness. The resulting salt occurs in white deliquescent prisms, or as a granular powder, which are readily soluble in water.

The Pharmacopœia demands the absence of monomethylarsenate, arsenate and phosphate, and requires that the salt shall contain not less than 72 per cent., nor more than 75 per cent. of pure anhydrous sodium dimethylarsenate, which latter is determined by titrating a solution of the salt, previously neutralized, if acid or alkaline, with normal hydrochloric acid in the same manner as directed for the assay of sodium borate, cacodylic acid, like boric acid, being indifferent to methyl orange. Each mil. (or Cc.) of normal hydrochloric acid required corresponds to 0.1600 Gm. of anhydrous sodium cacodylate.

Monohydrated Sodium Carbonate. $Na_2CO_3 + H_2O$.—This is the only form of sodium carbonate now recognized in the Pharmacopœia and is to be decidedly preferred to the efflorescent salt containing 10 molecules, or 62.93 per cent., of water of crystallization. It is also to be preferred to the dried sodium carbonate at one time official, as it represents, weight for weight, a larger proportion of sodium carbonate and contains less water. It may be made by crystallizing a solution of sodium carbonate at a temperature above 35° C. (95° F.), and is comparatively stable in the air. When exposed to warm dry air at or above a temperature of 50° C. (122° F.) it effloresces, and at 100° C. (212° F.) loses all of its water, 14.52 per cent.

The Pharmacopœia demands almost absolute purity for this salt, requiring that, when titrated with normal sulphuric acid, it shall contain not less than 99.5 per cent. of the monohydrated compound (equivalent to 85 per cent. of anhydrous sodium carbonate), each mil. (or Cc.) of normal acid consumed corresponding to 0.06201 Gm. of $Na_2CO_3 + H_2O$.

Sodium Chloride. NaCl.—There is probably no substance so universally distributed over the world as common salt, nature providing it both in crystalline form, as rock salt, or in solution, as sea water and the brine of salt wells. Rock salt is extensively mined, but the largest supply of salt is obtained by evaporation of the natural solutions. Enormous quantities of sodium chloride, for commercial purposes, are obtained by evaporation of the waters of the Great Salt Lake in Utah, which contain between 20 and 25 per cent. of the salt; the water is gotten rid of partly by spontaneous evaporation and partly by means of artificial heat in large reservoirs.

The Pharmacopœia demands for the official salt the absence of bromides and iodides and limits the presence of calcium and magnesium chlorides to mere traces. It also requires that, when dried to constant

weight at 110° C. (230° F.), it shall contain not less than 99 per cent. of pure sodium chloride, to be determined by titration with tenth-normal silver nitrate solution, each mil. (or Cc.) of which corresponds to 0.05846 Gm. of pure NaCl.

Sodium chloride is employed in the manufacture of certain chemicals, but is used rarely in medicine, although an indispensable requisite in the animal system. It is of chief interest to pharmacists in the preparation of physiological salt solution and as a reagent in the volumetric valuation of silver salts. Commercial sodium chloride sold as table salt is sometimes contaminated with magnesium chloride, which accounts for its hygroscopic character.

Sodium Citrate. $Na_3C_6H_5O_7 + 2H_2O$.—This salt is rarely used in medicine, although identical with potassium citrate in therapeutic value, but has received recognition in the Pharmacopœia because it is used in some official preparations. The present official salt differs from that heretofore recognized in containing far less water of crystallization, only 12.21 per cent. as against 27.74 per cent. of the former salt. Small quantities of the salt are sometimes required and may be readily made by neutralizing a solution of citric acid with monohydrated sodium carbonate or sodium bicarbonate; 100 parts (grams or grains) of the official salt require 71.5 parts of citric acid and 63.25 parts of monohydrated sodium carbonate or 85.7 parts of sodium bicarbonate, the resulting solution being either allowed to crystallize or evaporated to a dry granular condition.

The Pharmacopœia requires that the official sodium citrate shall contain not less than 98 per cent. of the crystallized salt, which is determined in exactly the same manner as directed for the assay of potassium citrate. Each mil. (or Cc.) of half-normal sulphuric acid corresponds to 0.04901 Gm. of $Na_3C_6H_5O_7 + 2H_2O$.

Sodium Cyanide. NaCN.—This salt is now officially recognized in place of potassium cyanide, and may be made by different processes. Large quantities are obtained by fusing sodium carbonate with calcium cyanamide, CaN.CN, leaching the melt with hot water, filtering and evaporating the solution. A very pure product may be made by passing hydrocyanic acid gas into an alcoholic solution of sodium hydroxide, when the newly formed sodium cyanide will separate as a bulky crystalline precipitate which may be washed on a filter with alcohol.

Sodium cyanide must be preserved in tightly closed bottles, for while odorless when dry, it is deliquescent when exposed to air and exhales the odor of hydrocyanic acid.

The Pharmacopœia requires that the salt shall contain not less than 95 per cent. of pure NaCN, which is determined by titration with tenth-normal silver nitrate solution in the presence of ammonia water. The potassium iodide added in the official assay serves as an indicator and

as sodium cyanide forms with silver nitrate a soluble double cyanide of silver and sodium, as shown by the equation $2NaCN + AgNO_3 = NaAg(CN)_2 + NaNO_3$, no precipitate will appear until one-half of the sodium cyanide has been acted upon by the silver nitrate, after which the solution becomes cloudy by precipitation of silver iodide insoluble in the ammonia water. From the above equation it follows that 2 molecules, or 98.02 Gms., of sodium cyanide react with 1 molecule, or 169.89 Gms., of silver nitrate, and hence each mil. (or Cc.) of tenth-normal silver nitrate solution containing 0.016989 Gm. of silver nitrate must correspond to 0.009802 Gm. of pure sodium cyanide.

Sodium Glycerophosphate. $Na_2C_3H_7PO_6$ **or** $C_3H_5(OH)_2PO_4Na_2$.—Until recently, 1911, sodium glycerophosphate was found on the market only in the form of a pasty mass claimed to contain 75 per cent. of the salt, but is now obtainable in crystalline form containing variable proportions of water. The process by which the crystalline product is obtained has not been published, although it is stated that in the manufacture of the salt two varieties of sodium glycerophosphate are obtained, one occurring as a slightly yellowish syrup, which when dried completely forms a very hygroscopic porous mass, and the other a permanent crystalline product.

The Pharmacopœia requires that the official salt shall contain not less than 68 per cent. of pure anhydrous sodium glycerophosphate, which is determined in the same manner as directed for the assay of borax and sodium cacodylate, by titration with half-normal hydrochloric acid, each mil. (or Cc.) of which corresponds to 0.10805 Gm. of anhydrous sodium glycerophosphate, the liberated glycerophosphoric acid, like boric and cacodylic acids, being indifferent to methyl orange.

Sodium Hydroxide. NaOH.—The usual method of manufacture of sodium hydroxide, or caustic soda, as it is commonly called, is by decomposition of a solution of sodium carbonate by means of milk of lime, the filtrate, as in the case of caustic potash, being evaporated in silver or iron vessels, and finally allowed to congeal in suitable moulds. The product thus obtained is commercially known as soda by lime. A purer article may be obtained either by purification of commercial caustic soda with alcohol or by direct action of metallic sodium on pure water. Large quantities of sodium hydroxide are now made electrolytically from sodium chloride, both in this country and abroad.

Like potassium hydroxide, sodium hydroxide is very deliquescent, and rapidly absorbs carbon dioxide upon exposure to the air; hence the same care must be observed in its preservation in tightly stoppered green glass bottles.

The Pharmacopœia requires that the official sodium hydroxide shall contain not less than 90 per cent. of pure NaOH, which is determined exactly in the same manner as directed for the assay of potassium

hydroxide, by titration with normal hydrochloric acid, each mil. (or Cc.) of which corresponds to 0.04001 Gm. of NaOH.

Sodium Hypophosphite. $NaH_2PO_2 + H_2O$.—Like the corresponding potassium salt, this salt may be conveniently made by decomposing a solution of calcium hypophosphite with sodium carbonate or sulphate. After removal of the calcium salt by filtration the solution is evaporated on a waterbath to dryness, with constant stirring for the purpose of granulation.

Sodium hypophosphite is hygroscopic, but more permanent than the potassium salt upon exposure to air, and explodes readily when triturated with nitrates, chlorates, or permanganates, owing to its tendency to oxidation.

The Pharmacopœia requires that the official sodium hypophosphite, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 98 per cent. of the hydrated salt, which is determined in exactly the same manner as directed for the assay of potassium hypophosphite by oxidation with nitric acid and subsequent titration with tenth-normal silver nitrate solution; in making the final calculation a different factor must be used, since each mil. (or Cc.) of tenth-normal silver nitrate solution corresponds to 0.0035357 Gm. of $NaPH_2O_2 + H_2O$.

Sodium Indigotindisulphonate.—This compound, also known as *Indigo Carmine*, and recognized in the French Pharmacopœia as Soluble Indigo, is chiefly the sodium salt of indigotindisulphonic acid, $C_{16}H_8O_2N_2(SO_3Na)_2$. It may be prepared by adding a sodium salt to a solution of soluble indigo, indigotindisulphonic acid, and washing the resulting precipitate with a solution of the same salt. Indigo carmine occurs as a blue powder or as a dark purple paste, sparingly soluble in water and almost insoluble in alcohol.

While the Pharmacopœia makes no requirement for a definite purity percentage, it demands the absence of iron ferricyanide and ferrocyanide, starch and starch iodide, and gives appropriate tests for the presence of these impurities or fraudulent additions.

There seems to be little or no occasion for official recognition of indigo carmine in the Pharmacopœia, since its use is practically confined to that of a dye for such products as mercuric chloride tablets, etc.

Sodium Iodide. **NaI.**—This salt may be obtained by processes analogous to those by which potassium iodide is made, but unlike the latter it is capable of combining with nearly 20 per cent. of water of crystallization. The official salt is anhydrous, but on exposure to air gradually absorbs moisture, which, however, is limited to 7 per cent. by the Pharmacopœia. The anhydrous salt is obtained by crystallizing at a temperature above 40° C. (104° F.) and when strong solutions of it in water are made, a decided rise of temperature is observed,

due to chemical union of the salt with water in its effort to form the hydrated salt $NaI + 2H_2O$.

The Pharmacopœia requires that sodium iodide, when dried to constant weight at 100° C. (212° F.), shall lose not more than 7 per cent. (due to moisture), and shall contain, in the dried state, not less than 99 per cent. of pure sodium iodide, which is determined by titration with tenth-normal silver nitrate solution, each mil. (or Cc.) of the latter corresponding to 0.014992 Gm. of anhydrous sodium iodide.

Sodium iodide, as well as its aqueous solution, gradually undergoes decomposition upon exposure to light, becoming colored, hence both should be preserved in dark amber-colored bottles.

Sodium Nitrite. $NaNO_2$.—This salt is interesting chiefly as the source of nitrous acid in the official process for the manufacture of ethyl nitrite in the preparation of spirit of nitrous ether. When sodium nitrate is heated with charcoal, starch, or similar reducing agents, sodium nitrite is formed; but a better process consists in heating fused sodium nitrate for some time with lead in thin sheets, whereby the lead is gradually converted into lead oxide or litharge and the sodium salt is reduced to nitrite; thus, $2NaNO_3 + Pb_2 = 2NaNO_2 + 2PbO$. The fused mass is lixiviated with water, the solution treated with carbon dioxide to remove any lead possibly held in solution, filtered, and finally allowed to crystallize. By repeated recrystallization a very pure salt can be obtained containing 98 per cent. and over of absolute sodium nitrite.

On account of its deliquescent character and ready oxidation to nitrate upon exposure to air, the salt must be carefully preserved in tightly closed bottles.

The Pharmacopœia requires that sodium nitrite, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 95 per cent. of pure $NaNO_2$, which is determined by adding a solution of the previously dried salt to a definite quantity of tenth-normal potassium permanganate solution and titrating the excess of the latter by means of tenth-normal oxalic acid solution. The equation $5NaNO_2 + 2KMnO_4 + 3H_2SO_4 = 5NaNO_3 + K_2SO_4 + 2MnSO_4 + 3H_2O$ shows that 5 molecules, or 345.05 Gms., of absolutely pure sodium nitrite require 2 molecules, or 316.06 Gms., of potassium permanganate for complete oxidation, and hence each mil. (or Cc.) of tenth-normal potassium permanganate solution containing 0.0031606 Gm. of the permanganate is capable of oxidizing 0.0034505 Gm. of pure sodium nitrite.

Sodium Perborate. $NaBO_3 + 4H_2O$.—This salt, according to German patent specifications, is obtained by adding a mixture of boric acid and sodium peroxide slowly to water acidified with sulphuric acid, or by adding boric acid to a concentrated aqueous solution of

sodium peroxide kept cold by addition of ice and then passing carbon dioxide through the mixture; the last named process is said to yield better results. The crystals which separate are washed with alcohol and dried at 58° C. (136.4° F.).

The Pharmacopœia requires that the official salt shall contain not less than 9 per cent. of available oxygen, corresponding to about 86.5 per cent. of crystallized sodium perborate, which is determined by dissolving a definite weight of the salt in water, acidulating with sulphuric acid, and titrating with tenth-normal potassium permanganate solution. When sodium perborate is added to water, oxygen is given off and forms hydrogen dioxide, while sodium metaborate remains in solution. The equations $NaBO_3.4H_2O + H_2O = H_2O_2 + NaBO_2 + 4H_2O$ and $5H_2O_2 + 2KMnO_4 + 3H_2SO_4 = 2O_5 + K_2SO_4 + 2MnSO_4 + 8H_2O$ show that 1 molecule, or 154.06 Gms., of sodium perborate yielding 1 atom, or 16 Gms., of oxygen forms 1 molecule, or 34.016 Gms., of hydrogen dioxide requiring 63.212 Gms. of potassium permanganate for determination of the latter; hence each mil. (or Cc.) of tenth-normal permanganate solution, containing 0.0031606 Gm. of potassium permanganate, consumed must correspond to 0.0008 Gm. of oxygen, or about 0.007703 Gm. of crystallized sodium perborate.

Sodium Phenolsulphonate. $NaSO_3C_6H_4(OH) + 2H_2O$ or $C_6H_4(OH)SO_2ONa + 2H_2O$.—This salt was at one time official under the name Sodium Sulphocarbolate and is still so designated occasionally. When pure phenol is mixed with an equal weight of sulphuric acid, a new compound is formed, to which the name sulphocarbolic or sozolic acid, or more correctly speaking, phenolsulphonic acid, has been given, and which has the composition $HSO_3C_6H_4(OH)$ or $C_6H_4(OH)SO_2OH$; the acid is monobasic and is produced according to the equation $C_6H_5(OH) + H_2SO_4 = HSO_3C_6H_4(OH) + H_2O$, the group SO_2OH displacing an atom of hydrogen in the benzene nucleus and not in the hydroxyl group. Two varieties of this acid are known, the ortho- and paraphenolsulphonic acids, the formation of which depends upon the temperature at which the reaction is allowed to go on; in the cold, only the ortho variety is produced, while with moderate heat a mixture of the ortho and para acids results, and at the temperature of boiling water only the para acid is obtained. Both varieties form clear solutions with water, but differ from each other in the character of their salts, both as regards solubility, form and constitution of the crystals.

The Pharmacopœia recognizes only the *para*-phenolsulphonate of sodium, which is prepared by heating a mixture of equal weights of phenol and sulphuric acid on a boiling waterbath for six hours, diluting the new compound with water, and neutralizing the hot liquid with an excess of barium carbonate. After filtration the solution of barium phenolsulphonate is decomposed by means of sodium carbonate, filtered, concentrated, and set aside to crystallize. The decomposition

involves a very simple reaction; thus, $Ba(SO_3C_6H_4(OH))_2 + Na_2CO_3 = 2NaSO_3C_6H_4(OH) + BaCO_3$. Lead carbonate may be used in place of the barium carbonate to neutralize the newly formed phenolsulphonic acid, as lead phenolsulphonate is also soluble in water.

The Pharmacopœia requires that the official salt shall contain not less than 83.64 per cent. nor more than 87.82 per cent. of anhydrous sodium paraphenolsulphonate, corresponding to not less than 99 per cent. of the crystallized salt, which is determined by titration with tenth-normal bromine solution. Four separate reactions occur in the official assay, thus: 1. The hydrochloric acid liberates bromine from the tenth-normal solution to the extent of 0.007992 Gm. for every mil. (or Cc.) of the latter added. 2. Two molecules of bromine, or 319.68 Gms., act upon 1 molecule of sodium phenolsulphonate, or 232.14 Gms., forming with it a dibromide and hydrobromic acid thus, $2Br_2 + C_6H_4(OH)SO_3Na + 2H_2O = C_6H_2Br_2(OH)SO_3Na + 2HBr + 2H_2O$. 3. The excess of bromine liberated reacts with the potassium iodide setting free a corresponding quantity of iodine. 4. The liberated iodine is taken up by titration with sodium thiosulphate solution. It is important that the flask be quickly stoppered after addition of the hydrochloric acid, to prevent the escape of bromine, and that the mixture be allowed to stand for not less than 10 nor more than 15 minutes, since longer contact with bromine causes the formation of tribromophenol, indicated by a turbidity or flocculent precipitate. The number of mils. (or Cc.) of tenth-normal sodium thiosulphate solution required, subtracted from 50, the number of mils. (or Cc.) of bromine solution added in the official assay, leaves the number of mils. (or Cc.) of the latter needed for the sodium phenolsulphonate present, and as each molecule, or 232.14 Gms., of crystallized sodium phenolsulphonate must yield 1 molecule, or 196.11 Gms., of the anhydrous salt, each mil. (or Cc.) of tenth-normal bromine solution, corresponding to 0.058035 Gm. of the crystallized salt, must also correspond to 0.04903 Gm. of the anhydrous salt. Finally the number of mils. (or Cc.) of tenth-normal bromine solution consumed by the sodium phenolsulphonate, when multiplied by 4.903 (0.04903×100) and divided by the weight of the salt originally taken, will express the percentage of anhydrous sodium phenolsulphonate present in the sample.

Sodium Phosphate. $Na_2HPO_4+12H_2O$.—Phosphoric acid, being tribasic, is capable of yielding three classes of alkali salts, known respectively as primary, secondary, and tertiary alkali phosphate. The official salt, as shown by the chemical formula, is the secondary or disodium hydrogen phosphate, which usually shows a neutral or only faintly alkaline reaction toward litmus, the primary phosphate having an acid and the tertiary phosphate a decidedly alkaline reaction. Disodium orthophosphate, as the official salt is also known, is made by decomposing a solution of acid calcium phosphate with sodium carbonate. The calcium salt is obtained by digesting calcined bone, or

bone ash, with sulphuric acid, whereby the tricalcium phosphate (of which bone contains about 40 per cent.) is converted into acid calcium phosphate and calcium sulphate, the latter being precipitated; thus, $Ca_3(PO_4)_2 + 2H_2SO_4 = CaH_4(PO_4)_2 + 2CaSO_4$; the magma is then strained, and the resulting liquid, containing the acid calcium phosphate in solution, is mixed with sodium carbonate as long as precipitation occurs, whereby secondary sodium phosphate is produced, and remains in solution, while secondary calcium phosphate is precipitated and carbon dioxide expelled; thus, $CaH_4(PO_4)_2 + Na_2CO_3 = Na_2HPO_4 + CaHPO_4 + CO_3 + H_3O$. The mixture is filtered, and the filtrate concentrated and allowed to crystallize.

The official sodium phosphate contains 60.35 per cent. of water of crystallization, a portion of which, about one-fourth, is lost by efflorescence upon exposure to air; moreover, carbon dioxide is gradually absorbed, the salt being converted into monosodium phosphate and acid sodium carbonate; hence, it must be preserved in well-stoppered bottles, in a cool place. At the temperature of boiling water the salt can be made anhydrous; but when exposed in this condition it again absorbs water, gradually forming a salt of the composition $Na_2HPO_4 + 7H_2O$, containing about 47 per cent. of water, which is permanent.

The Pharmacopœia requires that the official sodium phosphate shall contain not less than 39.25 per cent. nor more than 44 per cent. of anhydrous disodium orthophosphate, corresponding to not less than 99 per cent. of the crystallized salt, which is determined by titrating a solution of the salt with tenth-normal silver nitrate solution in a neutral liquid; each mil. (or Cc.) of the silver solution required for precipitation of the sodium phosphate as trisilver phosphate corresponds to 0.004735 Gm. of the anhydrous salt. The official assay may be explained as follows: Crystallized sodium phosphate contains 60.3 per cent. of water and hence each molecule, or 358.24 Gms., must correspond to 142.048 Gms., of the anhydrous salt, for 358.24 — 216.192 = 142.048. The equation $Na_2HPO_4 + 3AgNO_3 = Ag_3PO_4 + 2NaNO_3 + HNO_3$ shows that 1 molecule, or 142.048 Gms., of anhydrous sodium phosphate requires 3 molecules, or 3 times 169.89 = 509.67 Gms., of silver nitrate for complete precipitation as trisilver phosphate, and 1 mil. (or Cc.) of tenth-normal silver nitrate solution, containing 0.016989 Gm. of the silver nitrate must therefore correspond to 0.004735 Gm. of anhydrous sodium phosphate.

Effervescent Sodium Phosphate.—This preparation contains about 20 per cent. of exsiccated sodium phosphate, equal to about 50 per cent. of the crystallized official salt, and has already been considered in the chapter on Granular Effervescent Salts (see page 476).

Exsiccated Sodium Phosphate.—This salt, representing about $2\frac{1}{2}$ times its weight of the official crystallized sodium phosphate, has been introduced chiefly for the purpose of being used in making the preceding

effervescent preparation, for which the crystallized salt is wholly unsuited, on account of the large quantity of water present. The Pharmacopœia directs that it shall be prepared by allowing the crystallized salt to effloresce in warm air for several days and then gradually raising the temperature to 100° C. (212° F.) until all moisture has been driven off. It is then reduced to fine powder, which must be preserved in tightly stoppered bottles, as it absorbs moisture from the air very readily.

The Pharmacopœia requires that exsiccated sodium phosphate, when dried to constant weight at 110° C. (230° F.), shall contain not less than 98 per cent. of pure Na_2HPO_4, which is determined in the same manner as directed for the assay of crystallized sodium phosphate, except that a smaller quantity of the previously dried exsiccated phosphate is used.

Sodium Salicylate. $NaC_7H_5O_3$ or $C_6H_4(OH)COONa$.—The official salt may be conveniently obtained by mixing sodium bicarbonate 10 parts and salicylic acid 16.5 parts with distilled water 10 parts, in a glass or porcelain vessel, and, when effervescence has ceased, evaporating the solution, at a temperature not exceeding 60° C. (140° F.), to dryness. It is essential that the solution be slightly acid; hence, if necessary, a trifling addition of salicylic acid may be made, since alkali salicylates, in the presence of an excess of alkali, absorb oxygen from the air and become colored. Sodium bicarbonate and pure monocarbonate are better suited than sodium hydroxide for neutralizing the acid, since strong bases are likely to form different salts with salicylic acid, such as $Na_2C_7H_4O_3$, although the acid is monobasic; these so-called secondary salicylates are less permanent and less soluble in water than the normal salts.

All contact with iron must be carefully avoided in the preparation of this salt, owing to the delicate reaction of salicylic acid with that metal, and filtration through ordinary filter paper will frequently color a solution of the salicylate; hence, cotton or glass wool is preferable for straining.

The Pharmacopœia demands almost absolute purity for this salt, and requires that, when dried to constant weight at 100° C. (212° F.), it shall contain not less than 99.5 per cent. of pure sodium salicylate, which is determined by thoroughly carbonizing the previously dried salt, boiling the residue with an excess of half-normal sulphuric acid and titrating the excess of acid with half-normal potassium hydroxide solution, each mil. (or Cc.) of the half-normal acid consumed by the alkaline residue corresponding to 0.08002 Gm. of pure $NaC_7H_5O_3$.

Sodium Sulphate. $Na_2SO_4 + 10H_2O$.—This salt is daily obtained as a by-product in numerous chemical processes, such as the manufacture of hydrochloric and nitric acids and magnesium carbonate, as well as the generation of carbon dioxide from sodium bicarbonate

with sulphuric acid, in the manufacture of carbonated waters. It is purified, if necessary, by recrystallization.

The official salt, commonly known as Glauber's Salt, contains 55.9 per cent. of water of crystallization and effloresces rapidly upon exposure to air.

The Pharmacopœia requires that the official salt shall contain not less than 43.64 per cent. nor more than 48 per cent. of anhydrous sodium sulphate, corresponding to not less than 99 per cent. of the crystallized salt, which is determined gravimetrically by adding hot barium chloride solution to a boiling solution of the salt, acidulated with hydrochloric acid, heating the mixture on a waterbath for 30 minutes, filtering, washing the precipitate, and then drying and igniting and weighing the same. Each Gm. of barium sulphate corresponds to 0.6129 Gm. of anhydrous or 1.3804 Gms. of the uneffloresced sodium sulphate, and hence the weight of barium sulphate obtained, when multiplied by 61.29 (0.6129×100) and divided by the weight of crystallized salt originally taken will express the percentage of anhydrous sodium sulphate present in the sample.

For convenience in dispensing, the German Pharmacopœia directs the preparation of dried sodium sulphate, by exposing the crystallized salt to a modern heat until its weight has been reduced to one-half, as in the case of dried sodium carbonate. The dehydrated salt is in the form of a white powder and represents about double the weight of the crystallized salt.

Effervescent sodium sulphate is directed by the British Pharmacopœia to be made from the anhydrous salt in the same manner as stated under sodium phosphate. It contains about 25 per cent. Na_2SO_4.

Exsiccated Sodium Sulphite. Na_2SO_3.—Since crystallized sodium sulphite loses all of its water of crystallization at a temperature somewhat above 100° C. (212° F.), the coarsely crushed crystals may be gradually heated until they cease to lose weight, or a solution of the crystallized salt may be evaporated with constant stirring until an anhydrous residue is left. It must be kept in tightly closed bottles, as it is gradually oxidized to sulphate on exposure to air.

The Pharmacopœia requires that the official salt shall contain no less than 90 per cent. of pure anhydrous sodium sulphite, which is determined by adding a definite weight of the salt to a given quantity of tenth-normal iodine solution, whereby the sodium sulphite is oxidized to sodium sulphate, and then titrating the excess of iodine solution with tenth-normal sodium thiosulphate solution; each mil. (or Cc.) of tenth-normal iodine solution consumed corresponds to 0.006304 Gm. of pure Na_2SO_3.

Sodium Thiosulphate. $Na_2S_2O_3 + 5H_2O$.—This salt, frequently but wrongly called sodium hyposulphite, may be obtained in various

ways, such as boiling a solution of sodium sulphite with sulphur ($Na_2SO_3 + S = Na_2S_2O_3$), adding iodine to a solution of sodium sulphite and sulphide ($Na_2SO_3 + Na_2S + I = Na_2S_2O_3 + 2Na_2S_5 + 3H_3O$), etc.; the process employed on a large scale, however, consists in decomposition of calcium thiosulphate in solution by means of sodium carbonate or sulphate, insoluble calcium carbonate or sulphate being precipitated, while sodium thiosulphate remains in solution and is recovered, after filtration, by crystallization; the reaction may thus be indicated, $CaS_2O_3 + Na_2CO_3 = Na_2S_2O_3 + CaCO_3$. Calcium thiosulphate is obtained either from the residue left in the manufacture of sodium carbonate by the Leblanc process, known as alkali-waste, or from the gas lime left in the purification of illuminating gas by dry lime. Both of these residues contain calcium sulphides which, upon exposure to the air, undergo oxidation and are converted into thiosulphate.

Unfortunately the name sodium hyposulphite, which was formerly also the official title for this salt, is still applied almost altogether commercially. True sodium hyposulphite has the formula $NaHSO_2$, and may be prepared by treating a solution of sodium bisulphite with metallic zinc, whereby sodium hyposulphite and sulphite, together with zinc sulphite, are formed; thus, $3NaHSO_3 + Zn = NaHSO_2 + Na_2SO_3 + ZnSO_3 + H_2O$; this salt is used by dyers and calico-printers. Hyposulphites can be distinguished from thiosulphates by heating them, when the former break up into thiosulphates and water, while the latter yield sulphates and sulphides.

The Pharmacopœia requires that the official salt shall contain not less than 63.07 per cent. nor more than 67.48 per cent. of anhydrous sodium thiosulphate, corresponding to not less than 99 per cent. of the crystallized salt, which is determined by titration with tenth-normal iodine solution, each mil. (or Cc.) of which corresponds to 0.015814 Gm. of anhydrous, or 0.024822 Gm. of crystallized sodium thiosulphate. The equation $I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$ shows that 1 molecule, or 253.84 Gms., of iodine requires 2 molecules, or 316.28 Gms., of anhydrous sodium thiosulphate for complete absorption, and hence each mil. (or Cc.) of tenth-normal iodine solution, containing 0.012692 Gm. of iodine will require 0.015814 Gm. of anhydrous sodium thiosulphate for complete decoloration.

Sodium thiosulphate is employed to a limited extent in medicine, but its chief use in pharmacy is as a valuable chemical reagent in volumetric analysis.

Solution of Sodium Chloride, Physiological.—This solution, also known as *Physiological Salt Solution* and *Normal Salt Solution*, might be looked upon as a 0.85 per cent. solution, since the Pharmacopœia directs that 8.5 Gms. of sodium chloride be dissolved in sufficient freshly distilled water to make 1000 mils. (or Cc.). It should be made only with sodium chloride conforming to the official

requirements and never with commercial table salt. In order that the solution may be sterile, it is directed to be boiled for 1 hour in a flask closed loosely with a pledget of cotton, and should not be used after it has been made 48 hours.

Solution of Sodium Glycerophosphate.—Since the Pharmacopœia requires this solution to contain not less than 50 per cent. of anhydrous sodium glycerophosphate, it may be prepared by dissolving 75 Gms. of the official crystallized sodium glycerophosphate (which is required to contain not less than 68 per cent. of the anhydrous salt) in 25 Gms. of distilled water, if necessary with the aid of a gentle heat, and adding sufficient distilled water subsequently, when cold, to restore the weight to 100 Gms.

Solution of Sodium Hydroxide.—This preparation closely resembles the official solution of potassium hydroxide, and can be made either by decomposing a solution of sodium carbonate with milk of lime or by dissolving sodium hydroxide direct in distilled water. The latter method is usually followed by pharmacists. The finished product has a specific gravity of 1.056 at 25° C. (77° F.). The official formula, which directs the solution of 56 Gms. of sodium hydroxide in 944 Gms. of water, assumes that sodium hydroxide of 90 per cent. NaOH content is available, and, if a stronger or weaker article must be used, either a lesser or greater quantity should be taken; the exact quantity necessary may be ascertained by dividing 5040 by the exact percentage of NaOH in the sample. As 56 Gms. at 90 per cent. is equal to 50.4 Gms. at 100 per cent., it will require as many Gms. of x per cent. strength as x per cent. is contained times in 50.4×100 or if x is represented by 84, the answer will be found by dividing 84 into 5040.

Solution of sodium hydroxide should contain not less than 4.5 per cent. by weight of absolute NaOH, equal to about 22 grains in each fluidounce, and, for reasons already stated in connection with solution of potassium hydroxide, must be preserved in green glass bottles with tightly fitting stoppers coated with paraffin. The strength of solution of sodium hydroxide is determined in the same manner as directed for the assay of solution of potassium hydroxide, by titration with normal hydrochloric acid, after treatment with barium chloride solution. Each mil. (or Cc.) of the normal acid consumed corresponds to 0.04001 Gm. of pure sodium hydroxide.

The official solution of sodium hydroxide of the German Pharmacopœia (Liquor Natri Caustici) contains 15 per cent., and that of the French Codex 23 per cent. of caustic soda.

Solution of Chlorinated Soda.—The Pharmacopœia directs that this solution shall be made by adding a hot solution of monohydrated sodium carbonate to a uniform aqueous suspension of chlorinated lime, whereby the calcium salts (chiefly calcium hypochlorite) are

decomposed and precipitated as calcium carbonate, while the corresponding sodium salts remain in solution. When cool the mixture is passed through a well wetted muslin strainer and kept in tightly stoppered bottles. The object of directing a hot solution of sodium carbonate to be used is to insure the formation of a dense precipitate of calcium carbonate, from which the liquid can be readily separated, otherwise much trouble will be experienced in filtration and washing.

The preparation is more familiarly known as Labarraque's Solution, and owes its value as a disinfectant to the *available* chlorine present. The solution should be preserved in dark bottles provided with rubber stoppers, as light is detrimental to its stability, and cork stoppers are gradually destroyed by the liquid. The escape of carbon dioxide upon the addition of hydrochloric acid to the solution is due to the decomposition of sodium carbonate, which is frequently present, owing to the variable composition of the chlorinated lime used in the manufacture.

The official solution is required to contain not less than 2.5 per cent. by weight of available chlorine, which is determined by liberating the chlorine with acetic acid and allowing the same to act upon potassium iodide; whenever chlorine is allowed to act upon potassium iodide, it displaces iodine in atomic proportions, $2KI + Cl_2 = 2KCl + I_2$; the iodine thus set free can be determined volumetrically with tenth-normal sodium thiosulphate solution, and from the quantity of this solution used the amount of liberated chlorine can be readily calculated. One atom, or 35.46 Gms., of chlorine being equal to 1 atom, or 126.92 Gms., of iodine, each mil. (or Cc. of the thiosulphate solution corresponding to 0.012692 Gm. of iodine, will also correspond to 0.003546 Gm. of chlorine.

A preparation very similar to the foregoing is the solution of chlorinated potassa known as Javelle water, or eau de Javelle; it is made by substituting an equivalent quantity of potassium carbonate for the sodium carbonate in the above process. A formula for its preparations is given in the *National Formulary*.

Solution of Sodium Arsenate.—Like Fowler's Solution, this preparation may be more conveniently considered with the official compounds of arsenic.

Among the salts of sodium not recognized in our Pharmacopœia are two which are official in the German Pharmacopœia, and prescriptions for which occasionally reach this country.

Sodium Arsanilate. $C_6H_4(NH_2)(AsO.OH.ONa) + 4H_2O$.—This salt is made by condensing aniline, $C_6H_5(NH_2)$, and arsenic acid, $AsO.(OH)_3$, when arsanilic acid, $C_6H_4(NH_2)(AsO.(OH_2)$, is formed with liberation of water. The newly formed arsanilic acid is neutralized with sodium carbonate and the solution concentrated and allowed to crystallize.

It occurs as a white, crystalline, odorless powder, soluble in 6 parts of water, and contains from 24.1 per cent. to 24.6 per cent. of arsenic, to which the chief medicinal value of the salt is due. The German Pharmacopœia applies the synonym Atoxyl to this salt.

Sodium Acetarsanilate, also known as Arsacetin. $C_6H_4(NH.CH_3CO)(AsO.OH.ONa) + 4H_2O$.—It is obtained from sodium arsanilate by replacing a hydrogen atom of the amino group by an acetyl radical, and occurs as a white, crystalline powder, soluble in 10 parts of cold, or 3 parts of warm water. Like sodium arsanilate, this salt owes its medicinal value to the arsenic present, of which it contains from 21.2 to 21.7 per cent.

CHAPTER XLIII.

THE COMPOUNDS OF LITHIUM.

THREE lithium salts are recognized in the Pharmacopœia. A peculiarity of all lithium salts, by which they can readily be distinguished from other alkali salts, is their complete solubility in a mixture of equal volumes of alcohol and ether, after conversion into the chloride.

The following is a list of the official lithium compounds:

Official English name.	Official Latin name.
Lithium Bromide,	Lithii Bromidum.
Lithium Carbonate,	Lithii Carbonas.
Lithium Citrate,	Lithii Citras.

Lithium Bromide. LiBr.—For the preparation of this salt diluted hydrobromic acid may be neutralized with lithium carbonate, or the latter salt may be agitated in a flask with a hot solution of ferrous bromide. The first method is probably the most desirable. Owing to the very deliquescent character of the salt it is not readily crystallized, and is preferably obtained in granular powder form by evaporating the solution to dryness on a waterbath.

Lithium bromide contains about 92 per cent. of bromine, a larger proportion than any other salt. It is very soluble in water and alcohol, and also soluble in ether, and must be carefully preserved in well-stoppered bottles.

The salt is likely to be contaminated with lithium chloride (due to chlorine in the bromine), and the Pharmacopœia requires not less than 85 per cent. of pure lithium bromide. The official test for the limit (about 1 per cent.) of other alkalies depends upon the solubility of lithium chloride in amyl alcohol, in which other alkali chlorides are insoluble. The 0.4 Gm. of lithium bromide directed in the test is capable of yielding, if absolutely pure, 0.195 Gm. of lithium chloride upon treatment with hydrochloric acid and chlorine test-solution, as indicated by the equation $LiBr + HCl = LiCl + HBr$, which shows that 1 molecule, or 86.86 Gms., of lithium bromide will yield 1 molecule, or 42.40 Gms., of lithium chloride, for 42.40×0.4 and divided by $86.86 = 0.195 +$; hence the limit of permissible residue insoluble in amyl alcohol, which has been fixed at 0.002 Gm. in the official test amounts practically to 1 per cent. calculated as alkali chloride.

The purity percentage of lithium bromide may be determined in the same manner as directed for potassium bromide, by titration with

tenth-normal silver nitrate solution, each mil. (or Cc.) of which corresponds to 0.008686 Gm. of pure LiBr.

Lithium Carbonate. Li_2CO_3.—The carbonate, the parent salt of the other lithium compounds, is obtained from the mineral lepidolite, a mixture of silicates and fluorides of potassium, sodium, aluminum, and lithium. By digestion with sulphuric acid impure lithium sulphate is obtained, which is freed from the other salts by crystallization, treatment with milk of lime, etc. The final solution of alkali hydroxides is mixed with ammonium carbonate, whereby the lithium carbonate is precipitated; or the mixed alkali hydroxides may be converted into chlorides, and the solution then treated with ammonium carbonate. For the purpose of purification lithium carbonate may be suspended in water and treated with carbon dioxide, when an acid carbonate, $LiHCO_3$, will be formed and enter into solution, upon heating which pure lithium carbonate will be precipitated.

Lithium carbonate is the least soluble of all alkali carbonates, and is, moreover, only a little more than half as soluble in boiling water as in cold water. It occurs in commerce as a light, odorless powder.

The Pharmacopœia demands that the salt, when dried to constant weight at 100° C. (212° F.), shall contain not less than 98.5 per cent. of pure Li_2CO_3, and that when dissolved in 40 times its weight of diluted acetic acid not more than 0.15 per cent. of insoluble residue shall remain. The purity percentage of lithium carbonate is determined by dissolving an accurately weighed quantity of the salt previously dried at 100° C. (212° F.) in an excess of normal sulphuric acid, and then titrating the excess of acid by means of normal potassium hydroxide solution, each mil. (or Cc.) of normal acid consumed corresponding to 0.03694 Gm. of pure Li_2CO_3.

Lithium Citrate. $Li_3C_6H_5O_7 + 4H_2O$ **or** $C_3H_4OH(COOLi)_3 + 4H_2O$. —This salt can be prepared by adding lithium carbonate to a solution of citric acid until the latter is neutralized, then concentrating the solution and allowing it to crystallize. As shown by the equation $2(H_3C_6H_5O_7 + H_2O) + 3Li_2CO_3 + 3H_2O = 2(Li_3C_6H_5O_7 + 4H_2O) + 3CO_2$, 2 molecules, or 420.16 Gms., of citric acid require 3 molecules, or 221.64 Gms., of lithium carbonate, the yield of crystallized lithium citrate being about 563.89 Gms. If the solution be evaporated to dryness and the residue heated to 140° C. (284° F.) an anhydrous salt will be obtained which was recognized in the Pharmacopœia of 1890.

The Pharmacopœia directs the permissible limit of other alkalies to be determined by carbonizing 0.4 Gm. of crystallized lithium citrate, heating the residue with hydrochloric acid for the purpose of converting it into chloride, and treating the latter with amyl alcohol. Each molecule of the crystallized citrate is capable, if absolutely pure, of yielding 3 molecules of lithium chloride, or 281.92 Gms. will

yield 127.2 Gms. of chloride, and hence the 0.4 Gm. of crystallized citrate ordered in the official test, if pure, can yield 0.1804 + Gm. of lithium chloride, of which amount not more than 0.004 Gm. is permitted to be insoluble in amyl alcohol and must be looked upon as alkali chlorides.

Not less than 98.5 per cent. purity is demanded for lithium citrate in crystallized form, to be determined in the manner directed for potassium citrate, by thoroughly carbonizing a definite weight of the salt, boiling the residue with an excess of half-normal sulphuric acid and titrating the excess of acid by means of half-normal potassium hydroxide solution; each mil. (or Cc.) of the half-normal acid consumed by the carbonate obtained corresponds to 0.4699 Gm. of pure crystallized lithium citrate.

Lithium Salicylate. $LiC_7H_5O_3$ or $C_6H_4(OH)COOLi$.—This salt is no longer recognized in the Pharmacopœia, but may be prescribed occasionally. The equation $Li_2CO_3 + 2(C_6H_4(OH)COOH) = 2C_6H_4(OH)COOLi + CO_2 + H_2O$ indicates that 1 molecule, or 73.88 Gms., of lithium carbonate reacting with 2 molecules, or 276.096 Gms., of salicylic acid will produce 2 molecules, or 287.96 Gms., of lithium salicylate, and hence 100 Gms. or grains of the salt can be conveniently made by suspending a mixture of 96 Gms. or grains of salicylic acid and 26 Gms. or grains of lithium carbonate in 250 mils. (or Cc.) of distilled water and heating the mixture until effervescence ceases and perfect solution results; the solution may then be filtered and evaporated to dryness.

CHAPTER XLIV.

THE COMPOUNDS OF AMMONIUM.

ALTHOUGH, thus far, all efforts to isolate the basylous radical of ammonium salts have failed, the existence of the hypothetical body NH_4 must be assumed, as, without it, it would be impossible to explain the formation and composition of a large and important class of compounds in accordance with accepted modern views regarding the replacement of hydrogen in acids. The decomposition of sodium amalgam by means of ammonium chloride, resulting in the production of sodium chloride and a new spongy amalgam having a metallic lustre, points strongly to the metallic character of the radical called ammonium. The indirect source of all ammonium salts is the gaseous body ammonia, NH_3, which may be looked upon as ammonium hydroxide minus water, $NH_4OH - H_2O = NH_3$; a characteristic feature of these salts is their complete volatilization upon application of heat.

The Pharmacopœia recognizes 7 salts of ammonium, 4 preparations of the salts, and 2 solutions of the hydroxide, as follows:

Official English name.	Official Latin name.
Ammonium Benzoate,	Ammonii Benzoas.
Ammonium Bromide,	Ammonii Bromidum.
Ammonium Carbonate,	Ammonii Carbonas.
Ammonium Chloride,	Ammonii Chloridum.
Ammonium Iodide,	Ammonii Iodidum.
Ammonium Salicylate,	Ammonii Salicylas.
Ammonium Valerate,	Ammonii Valeras.
Ammonia Water,	Aqua Ammoniæ.
Stronger Ammonia Water,	Aqua Ammoniæ Fortior.
Liniment of Ammonia,	Linimentum Ammoniæ.
Solution of Ammonium Acetate,	Liquor Ammonii Acetatis.
Aromatic Spirit of Ammonia,	Spiritus Ammoniæ Aromaticus.
Troches of Ammonium Chloride,	Trochisci Ammonii Chloridi.

Ammonium Benzoate. $NH_4C_7H_5O_2$ **or** $C_6H_5COONH_4$.—When benzoic acid is added to diluted ammonia water, the acid is neutralized and ammonium benzoate is formed, which, remaining in solution, may be obtained in colorless crystals, if the liquid be concentrated by aid of a moderate heat and set aside. As ammonium salts are readily decomposed by heat, the liquid should be kept alkaline by the occasional addition of ammonia water during evaporation. As shown by the equation $C_6H_5COOH + NH_3 = C_6H_5COONH_4$, 122.048 parts of benzoic acid, when neutralized by ammonia will yield 139.08 parts of ammonium benzoate, and hence to prepare 100 Gms. or grains

of the salt will require 87.76 Gms. or grains of benzoic acid and 123 Gms. or grains of official ammonia water containing 10 per cent. of ammonia gas.

The Pharmacopœia requires that ammonium benzoate, when dried for 24 hours in a desiccator over sulphuric acid, shall contain not less than 98 per cent. of pure $NH_4C_7H_5O_2$, which is determined by decomposing a solution of the previously dried salt with diluted sulphuric acid, extracting the liberated benzoic acid with chloroform, concentrating the latter solution, adding some previously neutralized diluted alcohol and titrating this solution with tenth-normal barium hydroxide solution, using phenolphthalein as indicator. Each mil. (or Cc.) of tenth-normal barium hydroxide solution required for neutralization corresponds to 0.013908 Gm. of $NH_4C_7H_5O_2$.

Ammonium Bromide. NH_4Br.—Decidedly the best method of preparing this salt is by double decomposition between boiling hot concentrated solutions of ammonium sulphate and potassium bromide, when, upon cooling, the newly formed potassium sulphate is precipitated, while ammonium bromide remains in solution. To facilitate removal of the potassium sulphate, alcohol is usually added to the cooled liquid. The salt may be obtained in granular form by decanting the solution, concentrating it, and evaporating to dryness with constant stirring.

Ammonium bromide may also be obtained quite pure by neutralizing somewhat diluted hydrobromic acid with ammonium carbonate or strong ammonia water, and evaporating the solution as directed above.

The Pharmacopœia demands that ammonium bromide, when dried to constant weight at 100° C., shall contain not less than 98.5 per cent. of pure NH_4Br, which may be determined volumetrically by adding to a solution of the previously dried salt an excess of tenth-normal silver nitrate solution and determining the excess by subsequent titration with tenth-normal potassium sulphocyanate solution. Each mil. (or Cc.) of tenth-normal silver nitrate solution is capable of precipitating 0.009796 Gm. of NH_4Br. The results of the assay will be accurate only in the absence of ammonium chloride, small quantities of which are likely to be present.

Ammonium Carbonate. $NH_4HCO_3NH_4NH_2CO_2$.—As shown by the chemical formula, the official salt is not the normal carbonate, which would have the composition $(NH_4)_2CO_3$, but is a mixture of acid ammonium carbonate and ammonium carbamate. It is obtained on an extensive scale by heating ammonium chloride with an excess of chalk and condensing the resulting vapors in leaden chambers; it is afterward resublimed. The decomposition is accompanied by the splitting off of ammonia and water; hence the composition of the sublimate, as given in the Pharmacopœia: $4NH_4Cl + 2CaCO_3 = NH_4HCO_3NH_4NH_2CO_2 + 2CaCl_2 + NH_3 + H_2O$.

Commercial ammonium carbonate is usually accompanied by empyreuma, to which its peculiar tarry odor is due, and for pharmaceutical purposes only the purified article should be employed. Owing to the rapid deterioration of the salt on exposure to air, from loss of both ammonia and carbon dioxide, it should be preserved in tightly closed bottles, the best container being a narrow-mouthed fruit jar provided with a rubber ring and metal clasp for hermetically sealing the glass top. Only firm translucent pieces of ammonium carbonate should be used, as the opaque friable condition is indicative of chemical change causing conversion of the salt into acid carbonate or bicarbonate.

When the official ammonium carbonate is dissolved in water it is converted into the so-called sesquicarbonate, a mixture of acid and normal carbonate; thus, $NH_4HCO_3NH_4NH_2CO_2 + H_2O = NH_4HCO_3(NH_4)_2CO_3$. The Pharmacopœia requires that the official salt shall yield not less than 30 per cent. nor more than 32 per cent. of ammonia gas. To determine the purity, 2 Gms. of the salt are dissolved in a mixture of 50 mils. (or Cc.) each of distilled water and normal sulphuric acid, and then titrating the excess of acid by means of normal potassium hydroxide solution, using methyl orange as indicator. Each mil. (or Cc.) of normal acid corresponds to 0.017034 Gm. of ammonia gas.

Ammonium Chloride. NH_4Cl.—Crude ammonium chloride is obtained by neutralizing the ammoniacal gas liquors, condensed in the preparation and purification of illuminating gas from coal, with hydrochloric acid, evaporating the solution to dryness and subliming the salt in iron vessels. This product, being usually contaminated with iron, is, for pharmaceutical purposes purified by adding ammonia water to a hot solution of the salt, filtering to remove the precipitated ferric hydroxide, and evaporating the filtrate with constant stirring, so as to form a granular powder.

The Pharmacopœia requires that the salt, when dried to constant weight at 100 C. (212 F.), shall contain not less than 99.5 per cent. of NH_4Cl, which is determined by titrating a solution of the previously dried salt with tenth-normal silver nitrate solution as described under Ammonium Bromide. Each mil. (or Cc.) of the tenth-normal silver solution corresponds to 0.005350 Gm. of NH_4Cl.

Ammonium Iodide. NH_4I.—This salt is most conveniently prepared by double decomposition between potassium iodide and ammonium sulphate dissolved in a small quantity of boiling water; when the mixture has cooled, alcohol is added to insure a more perfect separation of the newly formed potassium sulphate, and the solution of ammonium iodide is filtered and evaporated to dryness, constantly stirring. The reaction is as follows: $2KI + (NH_4)_2SO_4 = 2NH_4I + K_2SO_4$.

Ammonium iodide must be preserved in tightly stoppered dark bottles, as it is very hygroscopic and is readily decomposed when exposed to air and light. The salt should never be dispensed after it has become deeply colored, but may be restored to its original condition by dissolving in as little water as possible, adding solution of ammonium sulphide until the color is discharged, then filtering to remove the precipitated sulphur, and evaporating on a waterbath to dryness. The ammonium sulphide added undergoes decomposition, uniting with the free iodine to form ammonium iodide, while sulphur is precipitated at the same time; thus, $(NH_4)_2S + I_2 = 2NH_4I + S$.

The Pharmacopœia requires that ammonium iodide, when dried to constant weight at 100° C. (212° F.) shall contain not less than 99 per cent. of pure NH_4I, which may be determined volumetrically with tenth-normal silver nitrate solution as directed under Ammonium Bromide. Each mil. (or Cc.) of tenth-normal silver nitrate solution corresponds to 0.014496 Gm. of NH_4I.

Ammonium Salicylate. $NH_4C_7H_5O_3$ or $C_6H_4(OH)COONH_4$.—This salt is conveniently prepared by neutralizing ammonia water by means of salicylic acid and evaporating the solution to dryness. The equation $C_6H_4OHCOOH + NH_3 = C_6H_4OHCOONH_4$ shows that 138.05 parts of salicylic acid, when neutralized with ammonia water, will yield 155.08 parts of ammonium salicylate, and hence to prepare 100 Gms. or grains of the salt will require 89 Gms. or grains of salicylic acid and 110 Gms. or grains of official 10 per cent. ammonia water.

The Pharmacopœia requires that ammonium salicylate, when dried for 24 hours in a desiccator over sulphuric acid, shall contain not less than 98 per cent. of $NH_4C_7H_5O_3$, which is determined by decomposing a solution of the previously dried salt with diluted sulphuric acid, extracting the liberated salicylic acid with chloroform, concentrating the latter solution, adding some previously neutralized diluted alcohol and titrating this solution with tenth-normal barium hydroxide solution, using phenolphthalein as indicator. Each mil. (or Cc.) of tenth-normal barium hydroxide solution required for neutralization corresponds to 0.015508 Gm. of $NH_4C_7H_5O_3$.

Ammonium Valerate. $NH_4C_5H_9O_2$ or $(CH_3)_2CHCH_2COONH_4$.—This salt, also known as ammonium valerianate, is prepared by neutralizing pure valeric acid with ammonia, conducting the gas directly into the acid, so as to avoid the presence of water, which insures more perfect crystals.

When perfectly neutral, ammonium valerate has little disagreeable odor, but as the salt is prone to decomposition, it is frequently accompanied by the characteristic odor of valeric acid. The acid reaction sometimes observed in an aqueous solution of the salt is due to decomposition, which is indicated also by the pronounced odor of the free acid floating on the surface of the solution: valeric acid being mono-

basic, there can be no acid salt of the same; hence any free acid present is due to loss of ammonia in the normal salt.

The Pharmacopœia directs that the absence of ammonium acetate, which may possibly be present as an impurity, be determined by adding a weak solution of ferric chloride to a 5 per cent. solution of the salt and removing the precipitated ferric valerate by filtration; the filtrate must not be of a deep red color.

The salt is rarely prescribed except in the form of the elixir of ammonium valerate; in the preparation of this elixir it is customary to dissolve the salt in aromatic elixir, neutralizing any free acid present by means of ammonium carbonate.

Ammonium valerate must be carefully preserved in tightly stoppered vials.

Ammonia Liniment.—This popular preparation, better known as Hartshorn Liniment, is a soft ammonium soap (ammonium oleate) holding sesame oil in a state of more or less permanent emulsion. Sesame oil has been found to yield a much more satisfactory product than either cottonseed oil or olive oil.

Ammonia Water.—Under this name the Pharmacopœia recognizes an aqueous solution of ammonia containing 10 per cent. by weight of the gas. It is prepared, on a large scale, by liberating ammonia from ammonium chloride or sulphate, by the aid of lime and heat, and conducting the gas into a series of receivers containing cold water, where it is rapidly absorbed; the residue in the retort consists of either calcium chloride or sulphate, as the case may be; thus, $2NH_4Cl$ or $(NH_4)_2SO_4 + Ca(OH)_2 = 2NH_3 + (CaCl_2$ or $CaSO_4) + 2H_2O$. Ammonia water is also made by mixing the ammoniacal liquors of gas works with milk of lime, heating, and conducting the gas into water; when made by this process the solution generally is less pure, being accompanied by empyreuma.

Ammonia gas is very soluble in water, which at 0° C. (32° F.) is capable of taking up 1050 volumes of the gas, and even at 15° C. (59° F.) retains 727 volumes in solution. The official ammonia water contains about 125 volumes of gas—that is, 1 mil. (or Cc.) holds 125 mils. (or Cc.) of ammonia gas in solution.

Different grades of strength of ammonia water are found in commerce, of which that designated as 16° corresponds to the official 10 per cent. solution; but it must be borne in mind that ammonia water is prone to deteriorate, by loss of ammonia gas, when kept in loosely stoppered vessels, such as carboys, especially if stored in a warm place. Ammonia water should be preserved in glass-stoppered bottles, although sound corks may be used if not allowed to come in contact with the liquid, by covering with prepared bladder, as small particles of cork allowed to fall into the liquid soon impart a yellowish color to the same.

Ammonia water is frequently called *spirit of hartshorn* by the public; in the British Pharmacopœia it is recognized as *solution of ammonia,* and in the German Pharmacopœia as *solution of caustic ammonia.*

The strength of ammonia water is determined volumetrically with normal acid, each mil. (or Cc.) of which is capable of neutralizing 0.01703 Gm. of ammonia gas. The Pharmacopœia directs that about 5 mils. (or Cc.) of ammonia water, accurately weighed in a glass-stoppered bottle, be diluted with 50 mils. (or Cc.) of distilled water and then titrated with normal sulphuric acid, using litmus or methyl orange as indicator. The number of mils. (or Cc.) of normal acid required, when multiplied by 1.703 (0.01703 × 100) and divided by the weight of ammonia water taken for the assay, will express the percentage of ammonia gas present in the sample, which should be not less than 9.5 nor more than 10.5 per cent.

Stronger Ammonia Water.—This preparation differs from the preceding only in strength, containing 28 per cent. by weight of ammonia gas, and is prepared in a similar manner, except that the gas must be conducted into the cold water for a longer period of time, so that a greater amount may be absorbed.

Stronger ammonia water is not used in medicine, but has been found a very convenient source of supply for small quantities of pure ammonia gas, by simply heating in a flask provided with a delivery tube, and for this purpose has been officially recognized. It can also be employed for the manufacture of weaker solutions of ammonia, which can be prepared of any desired strength by diluting the stronger ammonia water with plain water in proper proportions by weight, as explained on page 80. On account of the readiness with which all solutions of ammonia part with the gas upon elevation of temperature, care should be exercised in opening bottles containing stronger water of ammonia, as serious accidents have been known to occur from the sudden expulsion of liquid upon loosening the stopper, due to accumulation of gas in the vessel.

The commercial grade known as 26° ammonia water corresponds to the official stronger solution. It should be purchased only in glass-stoppered bottles and preserved in a cool place. The official strong solution of the British Pharmacopœia, liquor ammoniæ fortis, contains 32.5 per cent. of ammonia gas (by weight).

The strength of the preparation is determined volumetrically, like that of the weaker ammonia water, with normal sulphuric acid, except that the Pharmacopœia directs that only about 2 mils. (or Cc.) of the stronger ammonia water, accurately weighed, be used for the assay. The official requirement is that stronger ammonia water shall contain not less than 27 per cent. and not more than 29 per cent. of ammonia gas.

Aromatic Spirit of Ammonia.—A hydro-alcoholic solution of normal ammonium carbonate, pleasantly flavored with essential oils. It contains 70 per cent. by volume of official alcohol, 1 per cent. of oil of lemon, and 0.1 per cent. each of oils of lavender and nutmeg. When official ammonium carbonate is treated with alcohol a portion of the salt enters into solution, the carbamate being converted into carbonate, while the acid carbonate remains undissolved; therefore the Pharmacopœia directs in the formula for this preparation that ammonia water shall be added to the ammonium carbonate before the admixture of the alcoholic solution of essential oils. This causes a change of the official salt into normal carbonate, which is perfectly soluble in alcohol; the change effected may be readily explained as follows: NH_4HCO_3-$NH_4NH_2CO_2 + NH_3 + H_2O = 2(NH_4)_2CO_3$. In order to insure the complete conversion of the ammonium salt, it has been found advantageous to allow the mixture of ammonium carbonate solution and ammonia water to stand for twelve or twenty-four hours and then to add to it the alcoholic solution of oils, otherwise a saline precipitate may form.

Since 157.12 parts of official ammonium carbonate will yield 192.17 parts of the normal carbonate, the finished solution, if properly made, will contain 41.58+ Gms. of the latter salt in a liter, or each mil. (or Cc.) will contain 0.0415+ Gm.

Solution of Ammonium Acetate.—This preparation, also known as Spirit of Mindererus, is an aqueous solution of ammonium acetate, containing also small amounts of acetic and carbonic acids. It should always be prepared fresh when wanted, as when kept on hand for some time it gradually loses carbon dioxide and absorbs ammonia from the air, finally acquiring an alkaline taste. Prepared according to the official formula, by dissolving 5 Gms. of ammonium carbonate (in firm pieces) in 100 mils. (or Cc.) of diluted acetic acid, the finished product will contain 0.0735+ Gm. of ammonium acetate in each mil. (or Cc.) (about 33 grains in each fluidounce), together with a trifling amount of acetic acid; to the latter, as well as to the carbon dioxide remaining in solution, the pleasant, refreshing taste of the preparation is due. 100 mils. (or Cc.) of diluted acetic acid contain 6.048 Gms. of absolute acetic acid, of which, according to the equation $NH_4HCO_3NH_4NH_2CO_2 + 3HC_2H_3O_2 = 3NH_4C_2H_3O_2 + H_2O + 2CO_2$, 5.731+ Gms. are required to saturate 5 Gms. of ammonium carbonate.

The official method of determining the strength of solution of ammonium acetate depends upon the liberation of ammonia gas by the addition of potassium hydroxide solution and passing the same by distillation into a measured quantity of normal sulphuric acid; the excess of acid is then titrated with normal alkali solution, using methyl orange as indicator. Each mil. (or Cc.) of the normal acid neutralized by the ammonia gas corresponds to 0.07707 Gm. of $NH_4C_2H_3O_2$.

CHAPTER XLV.

THE COMPOUNDS OF CALCIUM AND STRONTIUM.

THE compounds of these two metals used in pharmacy are comparatively few in number, and may be conveniently grouped together. The Pharmacopœia recognizes 10 compounds of calcium and 5 preparations of the same, but only 3 compounds of strontium. The following list embraces all that are officially recognized:

Official English name.	Official Latin name.
Calcium Bromide,	Calcii Bromidum.
Precipitated Calcium Carbonate,	Calcii Carbonas Præcipitatus.
Prepared Chalk,	Creta Præparata.
Calcium Chloride,	Calcii Chloridum.
Calcium Glycerophosphate,	Calcii Glycerophosphas.
Calcium Hypophosphite,	Calcii Hypophosphis.
Calcium Lactate,	Calcii Lactas.
Crude Calcium Sulphide,	Calcii Sulphidum Crudum.
Lime,	Calx.
Chlorinated Lime,	Calx Chlorinata.
Lime Liniment,	Linimentum Calcis.
Solution of Lime,	Liquor Calcis.
Syrup of Calcium Lactophosphate,	Syrupus Calcii Lactophosphatis.
Chalk Mixture,	Mistura Cretæ.
Compound Chalk Powder,	Pulvis Cretæ Compositus.
Strontium Bromide,	Strontii Bromidum.
Strontium Iodide,	Strontii Iodidum.
Strontium Salicylate,	Strontii Salicylas.

THE COMPOUNDS OF CALCIUM.

Calcium Bromide. $CaBr_2$.—The simplest method for the preparation of this salt is solution of calcium carbonate in hydrobromic acid, an excess of the former being added, the mixture filtered when effervescence has ceased, and the solution evaporated to dryness; a white granular powder is thus obtained, which is very deliquescent, and must be preserved in tightly stoppered bottles.

The Pharmacopœia defines the salt as a hydrated form of calcium bromide containing not less than 84 per cent. of pure $CaBr_2$, and limits the possible presence of magnesium and alkalies to about four-tenths of 1 per cent., by precipitating 10 mils. (or Cc.) of a 5 per cent. solution of the salt with ammonium oxalate test-solution; all calcium present will be precipitated as calcium oxalate and the filtrate on evaporation and ignition must not leave more than 0.004 Gm. of residue. It also directs that the purity percentage of the salt be determined in the same manner as in the case of potassium bromide;

each mil. (or Cc.) of tenth-normal silver nitrate solution consumed corresponds to 0.009995 Gm. of pure $CaBr_2$. In all quantitative determinations of calcium bromide, the salt should be carefully weighed in a stoppered weighing bottle, on account of its quick absorption of moisture when exposed to air.

Precipitated Calcium Carbonate. $CaCO_3$.—This salt, popularly known as precipitated chalk, is prepared by double decomposition between calcium chloride and sodium carbonate; solutions of the two salts are mixed and heated, when calcium carbonate is thrown down as a dense precipitate, while sodium chloride remains in solution. The decomposition may be illustrated as follows: $CaCl_2 + Na_2CO_3 = CaCO_3 + 2NaCl$; to remove the sodium chloride, the mixture is poured on a strainer and the precipitate washed with boiling water until the washings no longer indicate the presence of chlorine. It is then dried at 100° C. (212° F.).

If calcium carbonate be precipitated in the cold, it is flocculent and voluminous, in which condition it is difficult to wash it entirely free from the sodium chloride; hence the use of heat is advantageous. The precipitate consists of a micro-crystalline powder, entirely free, however, from grittiness.

The Pharmacopœia limits the presence of matter insoluble in a mixture of water and hydrochloric acid to one-fifth of 1 per cent., and the presence of soluble impurities to ½ per cent. It also requires that the salt, when dried to constant weight at 200° C. (392° F.), shall contain not less than 98 per cent. of pure $CaCO_3$, to be determined by precipitating the calcium, after conversion into chloride, with tenth-normal oxalic acid solution, in the presence of an excess of ammonia, at a temperature of 60° to 70° C. (140° to 158° F.), and ascertaining the excess of acid by titration of the filtrate with tenth-normal potassium permanganate solution; each mil. (or Cc.) of the tenth-normal oxalic acid solution consumed by the original solution corresponds to 0.0050035 Gm. of pure $CaCO_3$.

It is not adapted for internal use, but is employed in the preparation of other calcium compounds.

Prepared Chalk. $CaCO_3$.—The compound officially recognized under the name prepared chalk is native soft calcium carbonate, freed by elutriation from most impurities. Chalk occurs abundantly, as a soft earthy mineral, on the English coast, which, by repeated treatment with water, may gradually be freed from impurities and coarser particles. The process of elutriation has been fully explained on page 122. After collecting the suspended fine powder, the latter, while still moist, is formed into small nodular masses by means of a funnel and then dried.

The Pharmacopœia requires that when dried to constant weight at 200° C. (392° F.), prepared chalk shall contain not less than 97

per cent. of pure $CaCO_3$, which may be determined exactly in the same manner as directed for the assay of precipitated calcium carbonate.

Chemically, prepared chalk does not differ from the precipitated calcium carbonate, but, on account of its greater softness and adhesiveness, it is better adapted for internal administration, and is the kind of chalk used in the official chalk mixture. Although it is never so white, and is probably less pure than the preceding article, the latter should never be used in its place.

Calcium Chloride. $CaCl_2$.—This compound is extensively obtained in a crude state as a by-product in different chemical processes. It may be obtained pure either by dissolving pure calcium carbonate in pure hydrochloric acid or by dissolving ordinary chalk or marble in hydrochloric acid and freeing the solution from iron and other impurities by treatment with chlorine and subsequently milk of lime; the mixture is warmed and filtered, the filtrate being finally exactly neutralized with hydrochloric acid, evaporated to dryness and fused.

If a concentrated solution of calcium chloride be set aside to crystallize, a salt of the composition $CaCl_2 + 6H_2O$, containing nearly 50 per cent. of water, will be obtained; but if the solution be evaporated until a granular powder results, a very deliquescent white salt of the composition $CaCl_2 + 2H_2O$, containing about 25 per cent. of water, is produced. The Pharmacopœia recognizes only a hydrated form of calcium chloride containing not less than 75 per cent. of pure $CaCl_2$. To obtain the anhydrous salt, fusion at a temperature above 200° C. (392° F.) is necessary. Calcium chloride is very deliquescent and must be preserved in tightly stoppered bottles. The Pharmacopœia makes the same requirements for the possible presence of magnesium and alkalies in this salt, as in the case of calcium bromide and directs the purity percentage to be determined by titration with tenth-normal silver nitrate solution, each mil. (or Cc.) of which corresponds to 0.00555 Gm. of pure calcium chloride.

Calcium Glycerophosphate. $CaC_3H_7O_6P$ or $C_3H_5(OH)_2PO_4Ca$.—The official salt is the normal calcium salt of glycerophosphoric acid, obtained by neutralizing a solution of the acid with milk of lime, or calcium carbonate, filtering out any calcium phosphate formed, concentrating the filtrate in a vacuum apparatus and then precipitating the salt by addition of alcohol; for the purpose of purification the precipitated salt is further washed with alcohol, and then dried.

The Pharmacopœia limits the possible presence of alcohol-soluble impurities to 1 per cent. and requires that the salt, when dried to constant weight at 130° C. (266° F.), shall contain not less than 98 per cent. of pure $CaC_3H_7O_6P$, to be determined by igniting the salt, previously dried at 130° C. (266° F.), in a crucible until it ceases to lose weight; the residue consisting of calcium pyrophosphate should weigh not less than 59.2 per cent. of the dried salt taken. Two mole-

cules, or 420.33 Gms., of absolutely pure calcium glycerophosphate are capable of yielding 1 molecule, or 254.22 Gms. of calcium pyrophosphate, or 60.48 per cent. The determination of calcium content is also demanded and should be not less than 25.9 per cent.; it is ascertained by dissolving the previously dried salt in weak acetic acid, heating the solution to boiling and precipitating with an excess of ammonium oxalate solution; the precipitate of ammonium oxalate is washed, dried and ignited, yielding a residue of calcium oxide. If the anhydrous calcium glycerophosphate were absolutely pure, 1 molecule, or 210.17 Gms., would yield 1 molecule, or 56.07 Gms., of calcium oxide, equivalent to 26.67 per cent.

Calcium Hypophosphite. $Ca(PH_2O_2)_2$.—This salt, the parent salt of numerous other hypophosphites, is prepared by the direct action of phosphorus on calcium hydroxide in the form of milk of lime, phosphine, or hydrogen phosphide, being generated at the same time; $3Ca(OH)_2 + 6H_2O + P_8 = 3Ca(PH_2O_2)_2 + 2PH_3$. In order to avoid, as far as possible, the formation of the very annoying and spontaneously inflammable phosphine, E. Scheffer, as early as 1858, advocated the use of partially oxidized phosphorus, prepared by treating it under water with atmospheric air, whereby the phosphorus is changed to a spongy condition and combines more readily with lime, even at the ordinary temperature, but preferably if the mixture be heated to 55° C. (131° F.). When the reaction has ended, the mixture is filtered, the residue washed with water, and the united filtrates evaporated and granulated or allowed to crystallize.

Calcium hypophosphite is not hygroscopic, like the corresponding salts of potassium and sodium, and is very nearly as soluble in cold as in boiling water. The Pharmacopœia requires that the salt, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 98 per cent. of pure $Ca(H_2PO_2)_2$, and demands that not more than 0.5 per cent. of the salt shall be insoluble in water, indicating the permissible limit of phosphate. The purity percentage is determined in the same manner as directed for the assay of potassium and sodium hypophosphites, by first oxidizing the previously dried salt with nitric acid. Primary calcium phosphate, $Ca(H_2PO_4)_2$, is first formed, which is neutralized by sodium hydroxide solution yielding $CaHPO_4$ and Na_2HPO_4, which are then precipitated as trisilver phosphate by means of tenth-normal silver nitrate solution; each mil. (or Cc.) of the silver nitrate solution required corresponds to 0.002836 Gm. of pure $Ca(PH_2O_2)_2$. The explanation of the assay is practically identical with those given under Phosphoric Acid.

Calcium Lactate. $Ca(C_3H_5O_3)_2 + 5H_2O$.—This salt may be conveniently made by neutralizing a hot solution of lactic acid with calcium carbonate, filtering, and setting the filtrate aside to crystallize.

The Pharmacopœia demands the absence of salts of volatile fatty acids, as shown by warming a mixture of 0.5 Gm. of the salt with 1 mil. (or Cc.) of sulphuric acid, and limits the possible presence of magnesium and alkali salts to 1 per cent. When dried to constant weight at 120° C. (248° F.), the salt is required to contain not less than 98 per cent. of pure anhydrous calcium lactate, to be determined by incinerating the previously dried salt, which converts it into calcium carbonate, dissolving the residue in a definite quantity of half-normal hydrochloric acid, and then titrating the excess of acid by means of half-normal potassium hydroxide solution. The equations $Ca(C_3H_5O_3)_2 + O_6 = CaCO_3 + 2CO_2 + 5H_2O$ and $CaCO_3 + 2HCl = CaCl_2 + 2H_2O + CO_2$ show that 1 molecule, or 218.15 Gms., of pure anhydrous calcium lactate will yield upon incineration 1 molecule, or 100.07 Gms., of calcium carbonate capable of neutralizing 2 molecules, or 72.94 Gms., of hydrogen chloride (or absolute hydrochloric acid); hence each mil. (or Cc.) of half-normal hydrochloric acid, requiring 0.0250175 Gm. of calcium carbonate for neutralization, must correspond to 0.05454 Gm. of pure anhydrous calcium lactate.

Calcium Sulphide, Crude.—This preparation was formerly known as Sulphurated Lime (Calx Sulphurata, U. S. P., VIII Rev.), but the present official title is more in keeping with its true character, especially as it is required to contain not less than 55 per cent. of calcium monosulphide.

It is usually made by heating a mixture of exsiccated calcium sulphate, charcoal and starch in a crucible to bright redness until the black color has disappeared, after which the mixture is allowed to cool, is then powdered and at once transferred to bottles which must be kept tightly stoppered, as the compound gradually decomposes upon exposure to air. The equation $CaSO_4 + C_3 = CaS + 2CO + CO_2$ indicates the reaction occurring, calcium sulphide being formed with escape of carbon monoxide and dioxide; the starch used simply assists in the reduction of the calcium sulphate, which latter, however, is not complete, and the finished product contains some unchanged calcium sulphate and carbon in varying proportions.

Crude calcium sulphide occurs as a pale gray, sometimes yellowish, powder, which is only very slightly soluble in water and insoluble in alcohol, but is readily soluble in solutions of ammonium salts. The purity percentage is directed to be determined by first dissolving a small quantity, 0.2 Gm. of the compound in a solution of ammonium chloride in a glass-stoppered bottle, then decomposing this solution with a solution of cadmium chloride, adding acetic acid, warming the mixture on a waterbath, decanting the liquid, washing the precipitate with diluted acetic acid, adding tenth-normal iodine solution and moderately diluted hydrochloric acid, and finally titrating the excess of iodine with tenth-normal sodium thiosulphate solution.

Ammonium chloride solution is added in the official assay to facilitate

solution of the calcium sulphide present; the subsequent addition of cadmium chloride solution results in the formation of cadmium sulphide and calcium chloride. The object of adding acetic acid is to insure an acid medium in which the cadmium sulphide is precipitated without the risk of any of the latter being dissolved. Upon addition of the moderately diluted hydrochloric acid, soluble cadmium chloride is formed together with hydrogen sulphide, each molecule of the latter, resulting from 1 molecule of cadmium sulphide obtained from 1 molecule of calcium sulphide, subsequently reacting with 2 atoms of iodine to form hydriodic acid and liberating sulphur. The following equations will illustrate the various reactions: $CaS + CdCl_2 = CdS + CaCl_2$; $CdS + 2HCl = CdCl_2 + H_2S$; $H_2S + I_2 = 2HI + S$. It is thus seen that 2 atoms of iodine (or 253.84 Gms.) correspond to 1 molecule of calcium sulphide (or 72.14 Gms.), and hence each mil. (or Cc.) of tenth-normal iodine solution, containing 0.012692 Gm. of iodine, which disappears in the official assay, must represent 0.003607 Gm. of pure CaS.

Some commercial lots of crude calcium sulphide have been found to contain considerably more sulphide than the lowest limit given in the Pharmacopœia; as much as 70 per cent. of calcium sulphide has been obtained. The richer the calcium sulphide content, the higher the medicinal value of the product.

Lime. CaO.—Calcium oxide, also known as quicklime or caustic lime, is obtained by calcining calcium carbonate in suitable furnaces known as lime kilns. Oyster shells, limestone, marble, and other varieties of calcium carbonate are used for the purpose, the final product varying in quality according to the source; for pharmaceutical and chemical purposes, lime obtained by calcination of white marble is the most desirable, being less contaminated with impurities.

Good lime occurs in hard but porous masses, which, upon addition of half their weight of water, become heated and are converted into a soft white powder, known as slaked lime. The change is of a chemical nature, as is evidenced by the development of heat, resulting in the formation of calcium hydroxide: thus, $CaO + H_2O = Ca(OH)_2$. Since lime, upon exposure to air, gradually absorbs moisture and finally carbon dioxide, it must be preserved in well closed vessels in a dry place. Lime thus changed by exposure is called air-slaked lime.

The Pharmacopœia permits the presence of only slight traces of carbonate and demands the absence of more than 1 per cent. of matter insoluble in diluted hydrochloric acid. When ignited to constant weight, in a platinum crucible, with a blast lamp, official lime should not lose more than 10 per cent. in weight, indicating the permissible limit of volatile substances, and must then contain not less than 95 per cent. of pure CaO, which is to be determined in a solution made with diluted hydrochloric acid, by precipitation as ammonium oxalate by means of tenth-normal oxalic acid solution, as explained under Calcium

Carbonate, on page 612. Each mil. (or Cc.) of tenth-normal oxalic acid solution consumed corresponds to 0.0028035 Gm. of pure calcium oxide.

Lime is used in pharmacy as a dehydrating agent and for the preparation of the official solution of lime. When slaked and mixed with three or four times its weight of water it forms a smooth mixture or thin magma known as *milk of lime.*

Chlorinated Lime.—This compound, which owes its value entirely to the amount of available chlorine it contains, is prepared by exposing slaked lime on trays to the action of chlorine gas, care being taken that the temperature does not rise above 25° C. (77° F.), to avoid the formation of calcium chlorate. The views held by chemists regarding the nature of the compound formed differ, and the question has, at the present day, not been settled. Some contend that calcium hypochlorite, calcium chloride, and water are produced, according to the equation $2Ca(OH)_2 + Cl_4 = Ca(ClO)_2 + CaCl_2 + 2H_2O$, while others regard the dry product as having the composition $CaOCl_2$ or $CaCl(OCl)$, which, upon the addition of water, breaks up into calcium hypochlorite and chloride. The preponderance of opinion, at present, is in favor of the latter view, partly because the richest commercial samples of chlorinated lime or bleaching powder thus far produced do not contain the proportion of available chlorine (about 49 per cent.) which the compound $Ca(ClO)_2 + CaCl_2 + 2H_2O$ should yield.

The term "chloride of lime," usually applied to this substance in commerce, is a misnomer, probably given to it long before the chemical nature of the manufacturing process was understood.

Chlorinated lime always contains some calcium hydroxide, to which its partial insolubility in water is due. It should be kept in a cool, dry place, and protected from light, since the latter has a deleterious effect upon it, causing a loss of chlorine and oxygen, with production of calcium chlorate and chloride. If of good quality, chlorinated lime is not deliquescent, the latter phenomenon indicating decomposition.

Solutions of chlorinated lime should always be prepared, without heat, by triturating the powder in a mortar with successive portions of water and rapidly filtering through paper or cotton.

The Pharmacopœia requires that the official product shall contain at least 30 per cent. of available chlorine, which may be determined, by adding to a carefully prepared aqueous mixture of chlorinated lime, representing between 0.3 and 0.4 Gm. of the latter in 100 mils. (or Cc.), potassium iodide and acetic acid, and titrating the liberated iodine with tenth-normal sodium thiosulphate solution. The acetic acid decomposes the calcium hypochlorite present, liberating chlorine, which in turn sets free iodine in atomic proportions from the potassium iodide. Since 35.46 Gms. of chlorine will liberate 126.92 Gms. of iodine, each mil. (or Cc.) of tenth-normal sodium thiosulphate solution required

in the official assay and representing 0.012692 Gm. of iodine, must also correspond to 0.003546 Gm. of chlorine.

Solution of Lime.—This liquid, more familiarly known as lime water, is intended to be a saturated solution of calcium hydroxide. The official directions for its preparation are simple and easily followed: A convenient quantity of lime is slaked by the very gradual addition of 20 times its weight of distilled water and occasionally agitated during half an hour; after subsidence of the suspended particles the supernatant liquid is decanted and rejected, the object of this treatment being the removal of the more soluble impurities. The magma is then repeatedly washed on a filter with boiling water distilled until all traces of chloride have been removed, and mixed with cold distilled water, thoroughly shaken during 24 hours and transferred to bottles, the clear liquid being withdrawn when wanted.

It must not be supposed, however, that even the best lime will furnish unlimited quantities of good lime water, and the supply should be tested from time to time, either volumetrically, as directed by the Pharmacopœia, or empirically, by boiling a little of it in a test tube—in the latter case a turbid liquid should result, due to the separation of calcium hydroxide.

Lime water is a very important article in pharmacy, and should receive careful attention, as it is chiefly used as an antacid for infants. Pure lime, free from alum, should be used, and either distilled water or that which has been boiled and cooled. The supply of lime water should be kept in tightly corked bottles, in a cool place, as carbon dioxide is readily absorbed and heat is unfavorable to solution of the lime. Lime water is best decanted from the sediment—or, if filtered, this must be done under cover—the sediment should then be again well distributed in the liquid, by agitation, after the desired supply of solution has been withdrawn.

While a saturated aqueous solution of lime at 15° C. (59° F.) contains about 1.70 or 1.75 Gms. of calcium hydroxide in every liter, the official requirement of not less than 0.14 per cent. more nearly represents the average strength of good lime water as found in the drug stores. According to the equation $H_2SO_4 + Ca(OH)_2 = CaSO_4 + 2H_2O$, showing that 98.086 Gms. of hydrogen sulphate, or absolute sulphuric acid, are capable of neutralizing 74.09 Gms. of calcium hydroxide, each mil. (or Cc.) of the tenth-normal acid, containing 0.0049043 Gm. of H_2SO_4, required in the official assay, corresponds to 0.0037045 Gm. of pure $Ca(OH)_2$. Every 10 mils. (or Cc.) of lime water titrated will thus require not less than 3.8 mils. (or Cc.) of tenth-normal sulphuric acid to indicate the presence of not less than 0.14 per cent. of calcium hydroxide.

Syrup of Calcium Lactophosphate.—This syrup has been fully considered on page 271.

THE COMPOUNDS OF STRONTIUM.

Strontium Bromide. $SrBr_2 + 6H_2O$.—This salt may be prepared by neutralizing diluted hydrobromic acid with pure strontium carbonate added in excess, filtering the mixture, and evaporating the solution until crystals begin to form. Upon cooling, the salt separates in crystals, which should be dried at a moderate heat.

Since pure strontium carbonate is difficult to obtain, the use of pure strontium hydroxide has been suggested instead, as the latter may be prepared readily from the nitrate by converting it into oxide by calcination and then slaking this with water, removing any barium and calcium present by further appropriate treatment with water.

The official salt contains about 30.4 per cent. of water of crystallization, and deliquesces rapidly in moist air but effloresces in very dry air. It can be rendered anhydrous by heating to 120° C. (248° F.). The Pharmacopœia requires the absence of barium and, furthermore, that the salt shall contain not less than 98 per cent. of pure crystallized strontium bromide, which is determined by titration with tenth-normal silver nitrate solution in the same manner as directed for the assay of potassium bromide on page 569, except that 0.8 Gm. of the strontium salt are to be used instead of 0.4 Gm. ordered for potassium bromide. Each mil. (or Cc.) of tenth-normal silver solution consumed corresponds to 0.017778 Gm. of $SrBr_2 + 6H_2O$. The presence of chlorides and of calcium salts will necessarily increase the quantity of silver solution required.

Strontium Iodide. $SrI_2 + 6H_2O$.—Like strontium bromide, this salt may be prepared either from pure strontium carbonate or hydroxide by solution in the respective acid, but, since solution of hydriodic acid is rather unstable, it should be freshly prepared for the purpose. The process is identical with that for the preceding salt.

Strontium iodide is also deliquescent, but contains less water of crystallization (24.05 per cent.) than the bromide. By exposure to air and light it is colored yellow, and must, therefore, be preserved in dark, amber-colored bottles.

The Pharmacopœia demands at least 99 per cent. purity for the crystallized salt. In the official test, 1 Gm. of the salt, dissolved in water, is precipitated by addition of an excess of tenth-normal silver nitrate solution in the presence of nitric acid, the excess being determined by means of potassium sulphocyanate solution, using ferric ammonium sulphate as indicator. Each mil. (or Cc.) of the silver nitrate solution consumed corresponds to 0.022478 Gm. of $SrI_2 + 6H_2O$.

Strontium Salicylate. $Sr(C_7H_5O_3)_2 + 2H_2O$ or $(C_6H_4(OH)COO)_2Sr + 2H_2O$.—This salt may be prepared by suspending 10 parts of salicylic acid in 100 parts of hot water and gradually adding 5.34

parts of strontium carbonate free from iron; when effervescence has ceased the solution is filtered and then allowed to crystallize, or it may be evaporated to dryness.

The Pharmacopœia requires that this salt, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 99 per cent. of crystallized strontium salicylate, which is determined by thoroughly carbonizing about 2 Gms. of the previously dried salt, dissolving the residue in a definite quantity of half-normal hydrochloric acid, and titrating the excess of acid by titration with half-normal potassium hydroxide solution. Each mil. (or Cc.) of half-normal acid consumed by the carbonized residue corresponds to 0.099435 Gm. of $Sr(C_7H_5O_3)_2 + 2H_2O$.

Barium Compounds.—Although barium compounds are not recognized in the Pharmacopœia except as reagents, attention should be called to the use of barium sulphate, $BaSO_4$, by physicians in connection with *x*-ray diagnosis, as care must be exercised that it be not confounded with barium sulphide, BaS, and barium sulphite, $BaSO_3$, when prescribed in abbreviated form as Barii Sulph. Neither barium sulphide nor the sulphite is ever used in medicine, the former being sometimes employed as a depillatory and the latter used in the arts.

Barium sulphate can now be obtained absolutely pure and possesses some advantages over bismuth compounds, such as being lighter relatively than bismuth subcarbonate and passing more quickly through the stomach than the latter, when mixed with a test-meal. Only the kind sold in original packages and labeled "For X-ray Diagnosis" should be used.

While barium sulphate is insoluble in water and acid fluids, barium sulphide and sulphite are decomposed by the acid liquids of the stomach and then absorbed with poisonous effects; several deaths are on record due to confusion of the names.

CHAPTER XLVI.

THE COMPOUNDS OF MAGNESIUM.

ALTHOUGH the official magnesium salts are but few in number, they are extensively employed both by physicians and in domestic practice. The Pharmacopœia recognizes 6 compounds of magnesium, of which 2 are liquid preparations. The following comprise the list:

Official English name.	Official Latin name.
Magnesia Magma,	Magma Magnesiæ.
Magnesium Oxide (Magnesia),	Magnesii Oxidum.
Heavy Magnesia,	Magnesii Oxidum Ponderosum.
Magnesium Carbonate,	Magnesii Carbonas.
Magnesium Sulphate,	Magnesii Sulphas.
Solution of Magnesium Citrate,	Liquor Magnesii Citratis.

Magnesia Magma.—This popular preparation, better known as Milk of Magnesia, is directed by the Pharmacopœia to be made by adding a solution of sodium hydroxide to an aqueous suspension of magnesium carbonate with constant stirring, after which the mixture is agitated frequently during 15 minutes. In order to remove the sodium carbonate formed and any sodium hydroxide present, the magma is repeatedly washed with distilled water, the supernatant liquid being finally decanted until the suspended magma measures the required volume and then transferred to wide-mouthed bottles, which must be kept tightly stoppered and paraffined. The finished product represents magnesium hydroxide in a fairly permanent state of suspension.

The official formula, known as McNeary's formula, has proven somewhat unsatisfactory in the author's hands on account of the insufficient quantity of distilled water ordered for suspension of the magnesium carbonate. Unless the amount of water directed is increased at least 50 or 75 per cent., separation of the magnesium hydroxide takes place very slowly or not at all, and washing by decantation becomes practically impossible. Using the quantities directed in the official formula, the mixture failed to show any separation, even after standing at rest in a corked vessel for 60 hours. Since the first decantation removes only a comparatively small quantity of the original mother-liquor, repeated washing becomes necessary, and 8 or 10 washings have been found requisite before the washings respond to the official test with sulphuric acid.

The Pharmacopœia limits the possible presence of soluble impurities to 0.100 Gm. in 100 mils. (or Cc.) of the magma, and demands that

magnesia magma shall contain an amount of magnesium hydroxide in suspension corresponding to not less than 6.5 per cent., nor more than 7.5 per cent., which is determined by dissolving a definite weight of the magma in an excess of normal sulphuric acid and titrating the excess of acid with normal potassium hydroxide solution; each mil. (or Cc.) of the tenth-normal acid consumed corresponds to 0.02917 Gm. of magnesium hydroxide.

Magnesium Carbonate.—The Pharmacopœia defines this compound to be a mixture of hydrated magnesium carbonate and magnesium hydroxide, corresponding to not less than 39.2 per cent. of magnesium oxide and containing not more than 0.8 per cent. of calcium oxide. The exact composition will vary somewhat, but may be approximately represented by the formula $4MgCO_3 + Mg(OH)_2 + 5H_2O$.

Magnesium carbonate is prepared by mutual decomposition between solutions of magnesium sulphate or chloride, and of sodium carbonate; the composition of the resulting precipitate depends upon the concentration of the solutions employed, and the temperature at which the decomposition is effected and the precipitate dried. Pure normal magnesium carbonate is never obtained when a solution of the sulphate or chloride is mixed with an alkali carbonate, but always a basic carbonate, the proportion of normal carbonate present in the precipitate being greatest when dilute solutions are used at ordinary temperature.

If solutions of magnesium sulphate and sodium carbonate be mixed in the cold, no carbon dioxide is eliminated, a voluminous precipitate of basic magnesium carbonate being thrown down, while an acid magnesium carbonate, $MgH_2(CO_3)_2$, remains in solution; but if the solutions be mixed warm or hot, carbon dioxide is evolved. The reaction producing the official magnesium carbonate is probably as follows: $5(MgSO_4 + 7H_2O) + 5(Na_2CO_3 + H_2O) = (4MgCO_3 + Mg(OH)_2 + 5H_2O) + 5Na_2SO_4 + CO_2 + 34H_2O$, dilute solutions being used and mixed at a temperature not above 55° C. (131° F.); the precipitate is washed to remove sodium sulphate and dried without heat.

Both light and heavy magnesium carbonate occur in commerce, being manufactured extensively in this country and in England. The U. S. Pharmacopœia recognizes only the light variety, as indicated by the official description; this is also known as *magnesia alba*.

The Pharmacopœia limits the possible presence of soluble impurities to 1 per cent., which is determined by treating magnesium carbonate with boiling water, filtering the mixture and evaporating the filtrate to dryness. The determination of calcium content depends upon precipitation of any calcium carbonate present, after conversion into chloride, as calcium oxalate in the presence of ammonium chloride and ammonia, and final ignition of the precipitate with the aid of a blast lamp to constant weight; the calcium oxide thus obtained must not weigh more than 0.8 per cent. of the weight of magnesium carbonate

originally taken. Having determined the calcium oxide, the next step is to determine the quantity of normal sulphuric acid corresponding to the same by dividing the weight of oxide found by 0.028035, as each mil. (or Cc.) of the normal acid corresponds to 0.028035 Gm. of CaO. Now dissolve 1 Gm. of magnesium carbonate, accurately weighed, in 30 mils. (or Cc.) of normal sulphuric acid and titrate the excess of acid by means of normal potassium hydroxide solution. From the amount of normal acid consumed by the carbonate, subtract the amount of acid corresponding to the calcium oxide found in 1 Gm. and multiply the remainder by 0.02016 to get the weight of magnesium oxide represented by 1 Gm. of the carbonate. The amount of normal acid required by the magnesium compound present in the carbonate, should be not less than 19.44 mils. (or Cc.) indicating not less than 39.2 per cent. of MgO.

Magnesium Oxide. MgO.—The name calcined magnesia, by which this compound is commonly known, indicates the manner of its preparation. Magnesium carbonate is pressed somewhat firmly into a crucible and then heated to dull redness, whereby carbon dioxide and water are expelled, leaving about 42 per cent. of residue consisting of magnesium oxide. The process is known to be completed when a small quantity of the residue, suspended in water, no longer effervesces upon addition of an acid. The heat is not allowed to rise to full redness unless the powder can be kept constantly stirred, otherwise the magnesia is very apt to become granular. The following equation illustrates the change taking place: $4MgCO_3 + Mg(OH)_2 + 5H_2O = 5MgO + 4CO_2 + 6H_2O$.

Two varieties, a light and a heavy calcined magnesia, occur in commerce and are recognized in the Pharmacopœia, the former as Magnesii Oxidum, Light Magnesia, and the latter as Magnesii Oxidum Ponderosum, Heavy Magnesia. The two varieties are obtained in the same manner but from light and heavy magnesium carbonate respectively. Light magnesia is the kind generally used, and should invariably be employed when magnesia is to be dispensed in aqueous suspension; small quantities of water cannot be mixed with it without rendering it harsh and gritty, and, if 1 part of magnesia be added to 15 parts of water, the mixture will soon set to a gelatinous mass, hence care must be observed that sufficient water be used to overcome this tendency, and never should the water be added to the magnesia, but always the magnesia to the water. This peculiar behavior with water is due to the formation of gelatinous magnesium hydroxide, $Mg(OH)_2$, and is characteristic of light magnesia, heavy magnesia not readily uniting with water.

Light and heavy magnesia do not differ from each other chemically; the latter is a smoother and denser powder, preferred for use in powder mixtures on account of its smaller bulk.

The Pharmacopœia makes the same requirements for both the

light and the heavy oxides of magnesium, namely, that after ignition they shall contain not less than 96 per cent. of pure magnesium oxide and not more than 2 per cent. of calcium oxide; the permissible limit of water of hydration is also fixed in both cases at 10 per cent., being determined by noting the loss of weight when a definite weight of magnesia is exposed to a low red heat in a porcelain crucible. The calcium oxide content is determined exactly in the same manner as directed for its determination in magnesium carbonate, as is also the percentage of magnesium oxide present; in the latter case, each mil. (or Cc.) of normal sulphuric acid consumed corresponds to 0.02016 Gm. of pure MgO, and in the official assay, using 0.5 Gm. of calcined magnesia, not less than 47.62 mils. (or Cc.) of the normal acid will be necessary to indicate the required 96 per cent. of pure MgO.

Since magnesia absorbs moisture and carbon dioxide readily from the air, it must be preserved in tightly closed tin or glass vessels. The Pharmacopœia demands that only slight traces of carbonate shall be present, and not more than 2 per cent. of soluble salts.

Magnesium Sulphate. $MgSO_4 + 7H_2O$.—This salt, better known as Epsom Salt (a name given to it in connection with its first production at Epsom, England, in 1695), may be made from native magnesium carbonate, magnesite, by treatment with diluted sulphuric acid, but is obtained on a more extensive scale from kieserite, a native magnesium sulphate, found near Stassfurt, in Germany. The mineral is first heated by itself and then treated with boiling water, whereby the magnesium sulphate is brought into solution, being subsequently purified by crystallization.

Magnesium sulphate contains 51.16 per cent. of water of crystallization, and slowly effloresces on exposure to dry air. The small acicular or rhombo-prismatic crystals, in which form it occurs in commerce, are produced by agitation of the crystallizing solution, whereby the formation of large crystals is prevented.

The Pharmacopœia demands an almost absolutely pure product, allowing only slight traces of chlorides and requiring that official magnesium sulphate shall contain not less than 48.59 per cent., nor more than 53.45 per cent. of anhydrous magnesium sulphate, corresponding to not less than 99.5 per cent. of the pure crystallized sulphate. The latter is determined by precipitating a solution of a definite weight of the salt in distilled water by addition of an excess of sodium phosphate test-solution and after further addition of ammonia water, setting the mixture aside for 2 hours; the precipitate, which consists of ammonium magnesium phosphate, is thoroughly washed with diluted ammonia water, and then dried and ignited, whereby it is converted into magnesium pyrophosphate. Since 2 molecules, or 493.0 Gms. of crystallized, or 240.78 Gms. of anhydrous, magnesium sulphate will yield 1 molecule, or 222.72 Gms. of magnesium pyrophosphate, 1 Gm. of the latter salt must correspond to 1.08109 Gms.

of anhydrous magnesium sulphate or 2.2135 Gms. of the crystallized salt; the weight of magnesium pyrophosphate obtained in the official assay, therefore, if multiplied by 1.08109 will express the corresponding weight of anhydrous magnesium sulphate, and if multiplied by 2.2135 will express the corresponding weight of crystallized magnesium sulphate.

Several natural purgative waters, known as bitter waters, owe their therapeutic properties to the magnesium sulphate which they contain.

The German Pharmacopœia directs the preparation of dried magnesium sulphate, for dispensing purposes, in powder form. It is made by gradually heating crystallized magnesium sulphate on a water-bath until about two-thirds of the water has been expelled; the resulting white powder must be preserved in tightly corked bottles.

Solution of Magnesium Citrate.—This popular preparation is officially directed to be made by first dissolving 33 Gms. of citric acid in 150 mils. (or Cc.) of hot water and adding to this a mixture of 15 Gms. of magnesium carbonate and 100 mils. (or Cc.) of water. After complete solution has been effected, 60 mils. (or Cc.) of syrup are added, the mixture is heated to boiling and 0.1 mil. (or Cc.) of oil of lemon mixed with 5 Gms. of purified talc is added. After filtration, sufficient boiled water is added to nearly fill the bottle (of about 360 mils. (or Cc.) capacity) and when cool 2.5 Gms. of potassium bicarbonate are added and the bottle stoppered tightly. The magnesium carbonate and citric acid are ordered in the proper proportions for the formation of acid magnesium citrate, which is more soluble, and therefore remains in solution better than the normal citrate.

When the solution is made up for stock, trouble sometimes arises from the use of plain water, and fungi have been met with in the finished product after the lapse of some time, which renders the preparation unsightly and unsalable. This may be overcome by boiling and filtering the water to be used. As retention in the solution of all carbon dioxide, from the potassium bicarbonate, adds materially to the refreshing taste, the bottles should be securely stoppered and kept in a cool place, lying on the side. Unless patent stoppers are attached to the bottles, sound, soft corks only should be used, and, having first been swelled in water for an hour, they should be driven firmly into the neck of the bottles and then secured with twine or wire.

Tartaric acid and magnesium sulphate have on several occasions been found in solution of magnesium citrate, undoubtedly as fraudulent additions, and the Pharmacopœia demands the absence of both. The official requirement for strength of the solution is that it shall contain an amount of magnesium citrate equivalent to not less than 1.5 Gms. of magnesium oxide in 100 mils. (or Cc.), which is determined as follows: After a definite volume of the solution has been evaporated to dryness, it is thoroughly carbonized and the residue dissolved in diluted hydrochloric acid and filtered if necessary. To the filtrate

sodium phosphate test-solution is added and an excess of ammonia water, whereby the magnesium chloride formed is converted into ammonium magnesium phosphate; after thorough washing to insure removal of all chlorides, with diluted ammonia water, the precipitate is ignited to constant weight for the purpose of converting it into magnesium pyrophosphate. One molecule, or 222.72 Gms. of magnesium pyrophosphate is the equivalent of 2 molecules, or 80.64 Gms., of magnesium oxide, and hence 1 Gm. of the former must correspond to 0.36207 Gm. of the latter. Since the Pharmacopœia demands that 100 mils. (or Cc.) of solution of magnesium citrate shall contain magnesium citrate equivalent to 1.5 Gms. of magnesium oxide, the 10 mils. (or Cc.) used in the official assay should yield not less than 0.414 Gm. of magnesium pyrophosphate corresponding to 0.15 Gm. of magnesium oxide.

In connection with the preceding magnesium compounds another may be considered, because of its use in pharmacy, which is officially recognized under the name Talcum. Commercial talc, which is defined as a native hydrous magnesium silicate, occurs of varying degrees of purity, but in its natural state is not suitable for pharmaceutical work, and hence the Pharmacopœia directs the use of a purified article as a filtering medium.

Talcum Purificatum. Purified Talc.—The usual directions for preparing this filtering agent are intended to remove iron and such other impurities as may be soluble in the boiling water containing about 2 per cent. of hydrochloric acid. The treatment is repeated with a weaker acid, after which the insoluble residue is washed with water until all traces of the acid have been removed, and the purified talc is then dried at 110° C. (230° F.). When thus treated, purified talc should be entirely free from iron and upon ignition leave not less than 95 per cent. of residue. The limit of water-soluble impurities allowed is fixed by the Pharmacopœia at one-tenth of 1 per cent. Purified talc is an excellent filtering medium if used in powder of about No. 60, or No. 80, fineness, but the bolted varieties used for dusting purposes are unsuitable, as they will pass through the filter paper.

CHAPTER XLVII.

THE COMPOUNDS OF ALUMINUM AND CERIUM.

THERE are but 3 compounds of aluminum and 1 of cerium recognized in the Pharmacopœia, as shown by the following list:

Official English name.	Official Latin name.
Alum,	Alumen.
Exsiccated Alum,	Alumen Exsiccatum.
Aluminum Hydroxide,	Alumini Hydroxidum.
Cerium Oxalate,	Cerii Oxalas.

THE COMPOUNDS OF ALUMINUM.

Alum.—The general name alum is given to a class of salts, the characteristics of which are that they are double sulphates of a univalent and trivalent element, are isomorphous, crystallizing in the regular system of the cube and octahedron, and contain 12 molecules of water of crystallization. The univalent elements present may be either potassium, sodium, ammonium, cæsium, rubidium, or silver, while the trivalent element need not necessarily be aluminum, its place being sometimes taken by iron, chromium, or manganese, thus potassium alum, $AlK(SO_4)_2 + 12H_2O$; ammonium alum, $AlNH_4(SO_4)_2 + 12H_2O$; chrome alum, $CrK(SO_4)_2 + 12H_2O$; iron alum, $FeNH_4(SO_4)_2 + 12H_2O$, etc.

Crude alum occurs in nature in the form of alunite or alumstone, a mixture of aluminum hydroxide and aluminum and potassium sulphates; from this, as well as from alum-shale and the minerals cryolite and bauxite, official alum is obtained. Calcination and lixiviation, as well as treatment with sulphuric acid and addition of potassium sulphate or ammonium sulphate, are brought into requisition in the different processes, crystallization finally being employed for the purpose of purification. Owing to the presence of iron in the minerals from which alum is made, it is often found in the latter, but should not exceed traces, as determined by the official test with potassium ferrocyanide.

Official Alum. $AlNH_4(SO_4)_2 + 12H_2O$ and $AlK(SO_4)_2 + 12H_2O$.—The title alum is officially applied in the United States and British Pharmacopœias to both ammonium alum and potassium alum, whereas the German, French and Swiss Pharmacopœias recognize potassium alum only. The U. S. Pharmacopœia requires that the label of the container shall indicate whether the article is ammonium alum or potassium alum.

The two alums can be readily distinguished from each other by adding some potassium hydroxide solution to an aqueous 5 per cent. solution of the salt, when ammonia will be evolved in the case of ammonium alum; moreover potassium alum imparts a violet color to a non-luminous flame.

Ammonium alum is less soluble in water than potassium alum, but both alums lose their water of crystallization when heated to 200° C. (392° F.).

The Pharmacopœia requires that official alum shall contain not less than 99.5 per cent. of pure crystallized alum, which is determined by precipitating aluminum oxide from a given weight of the salt and then washing, drying and strongly igniting the same. Each Gm. of aluminum oxide thus obtained corresponds to 8.874 Gms. of crystallized ammonium alum, and to 9.286 Gms. of crystallized potassium alum.

Exsiccated Alum, also known as Dried Alum and Burnt Alum. $AlNH_4(SO_4)_2$ **or** $AlK(SO_4)_2$.—In the official process for preparing dried or exsiccated alum the crystals are first fused in a shallow capsule, the heat being then increased and continued until 10 parts have been reduced in weight to 5.5 parts and a white porous mass remains, which is preserved in powder form in tightly stoppered bottles. Official ammonium alum contains 47.89 per cent. of water of crystallization, while potassium alum contains 45.50 per cent. A temperature exceeding 200° C. (392° F.) must be avoided, to prevent decomposition and change of the aluminum sulphate to alumina, with loss of sulphuric acid.

Dried alum, although completely but slowly soluble in water, requires about twice as much water for solution as the crystallized alum.

The Pharmacopœia requires that when dried in an airbath at 150° C. (302° F.), exsiccated alum shall not lose more than 10 per cent. in weight (moisture), and after having been thus dried to constant weight, if precipitated by ammonia water, in the presence of ammonium chloride, thoroughly washed, dried and strongly ignited, the resulting aluminum oxide, Al_2O_3, shall correspond to not less than 98 per cent. of the previously dried exsiccated alum. Each Gm. of aluminum oxide corresponds to 4.643 Gms. of exsiccated ammonium alum, and to 5.055 Gms. of exsiccated potassium alum.

Aluminum Hydroxide. $Al(OH)_3$.—The Pharmacopœia directs this compound to be prepared by gradually pouring a hot solution of alum into a hot solution of monohydrated sodium carbonate, repeatedly washing the resulting precipitate with hot water, and finally drying the residue at a temperature not above 40° C. (104° F.). The decomposition is accompanied by the evolution of carbon dioxide, and may be illustrated as follows: $2(AlK(SO_4)_2 + 12H_2O) + 3(Na_2$-

$CO_3 + H_2O) = 2Al(OH)_3 + K_2SO_4 + 3Na_2SO_4 + 3CO_2 + 24H_2O$; this peculiar action is characteristic of certain metals—aluminum, iron in the ferric state, and chromium, the oxides of which exhibit weak basic properties and fail to combine with carbonic acid, but are precipitated as hydroxides when their soluble salts are acted upon by alkali carbonates.

The object of using hot solutions of the two salts and of adding the alum solution slowly to the alkaline liquid, is to prevent the formation of basic aluminum sulphate and to facilitate the complete removal of alkali and sulphuric acid, which would be persistently retained by the precipitated hydroxide if the precipitation took place in the presence of an excess of alum. The use of hot liquids also facilitates elimination of the carbon dioxide.

Drying the precipitate at a modern temperature is desirable to insure a smooth product, as a high heat would cause partial decomposition and a gritty powder.

Besides the official aluminum compounds the following are sometimes used:

Aluminum Sulphate. $Al_2(SO_4)_3 + 18H_2O$.—This salt is preferably prepared for medicinal purposes by dissolving freshly prepared aluminum hydroxide in a sufficient quantity of sulphuric acid properly diluted with water. An excess of acid should be avoided, as also an excess of the hydroxide; in the event of the latter, basic sulphates are likely to be formed. The gelatinous hydroxide will dissolve quite readily, and the solution having been filtered is evaporated on a water-bath until a crystalline residue is obtained.

Solution of Aluminum Acetate.—This preparation is recognized in the *National Formulary*, and is frequently prescribed as Liquor Burowii or Burow's Solution. It is made by adding a solution of lead acetate to a solution of aluminum sulphate, setting the mixture aside in a cold place for 24 hours, with occasional stirring and then decanting or syphoning off the clear liquid. The finished product contains about 5 per cent. of normal aluminum acetate, together with a trace of lead.

Solution of Aluminum Subacetate.—This solution, also recognized in the *National Formulary*, must not be confounded with the preparation previously mentioned. It contains a basic aluminum acetate, $Al_2(OH)_2(C_2H_3O_2)_4$, to the extent of about 7.5 or 8 per cent., and is made by mixing calcium carbonate with water and an insufficient quantity of acetic acid to effect solution; this mixture is added to a solution of aluminum sulphate and set aside for 24 hours with occasional stirring, the clear liquid being finally decanted and filtered. This preparation is practically identical with the official Liquor Aluminii Acetici of the German Pharmacopœia.

THE COMPOUNDS OF CERIUM.

Cerium Oxalate.—The official cerium oxalate is defined to be a mixture of the oxalates of cerium, didymium, lanthanum, and other associated elements, and hence no chemical formula is given for the salt. The impurities are of course present in very small proportions and in no way affect the therapeutic value of the compound. The process for obtaining cerium oxalate from the mineral cerite, its chief source, is somewhat complicated. The powdered mineral is digested with sulphuric acid, the mass dried and treated with diluted nitric acid and hydrogen sulphide, to remove copper and other metals. The cerite metals are next precipitated by means of oxalic acid and the mixed oxalates, after the addition, of magnesium carbonate, are calcined and the residue dissolved in a small quantity of concentrated nitric acid. The solution is poured into a large quantity of water containing about 0.5 per cent. of sulphuric acid, whereby the cerium is precipitated as yellow ceric sulphate, while lanthanum and didymium, together with the magnesium, remain in solution. The ceric sulphate is dissolved in sulphuric acid and reduced to cerous sulphate, by means of sodium thiosulphate, after which it is precipitated, as cerous oxalate, with oxalic acid and dried. Cerium oxalate may also be readily obtained by interaction between a soluble cerium salt (nitrate) and a soluble oxalate.

Cerium oxalate, as a rule, occurs as a white, granular powder, but sometimes has a pink color, due to the presence of larger proportions of didymium. When heated to redness it is decomposed leaving about 47 per cent. of a reddish-brown residue, consisting of ceric and other rare earth oxides. When pure, it has the formula $Ce_2(C_2O_4)_3 + 10H_2O$, as shown by Power and Sheddon.

CHAPTER XLVIII.

THE COMPOUNDS OF IRON.

THERE is no class of inorganic compounds, excepting the official preparations of the alkalies, more extensively employed in medicine than those of iron; they must therefore be considered as among the most important in the study of pharmacy. The Pharmacopœia recognizes, besides iron in the metallic form, no less than 18 different preparations of the same, of which 6 are liquid. Chemists have grouped all compounds of iron into two classes, designated as ferrous and ferric compounds, respectively, which differ from each other in striking physical and chemical properties; this distinction has also been maintained in the official titles of the iron salts and their solutions. Ferrous compounds, in which iron is bivalent, are, when not anhydrous, of a green color, with one exception, the yellow oxalate, and form a blue precipitate of ferrous ferricyanide, $Fe_3(Fe(CN)_6)_2$, known as Turnbull's Blue, with solution of potassium ferricyanide; ferric compounds, in which iron is trivalent, on the other hand, are characterized by a reddish- or yellowish-brown color and form a blue precipitate of ferric ferrocyanide, $Fe_4(Fe(CN)_6)_3$, known as Prussian Blue, with solution of potassium ferrocyanide.

The following is a list of the official preparations of iron, divided, for convenience, into three classes:

Official English name.	Official Latin name.
Metallic Iron.	
Iron,	Ferrum.
Reduced Iron,	Ferrum Reductum.
Ferrous Compounds.	
Ferrous Sulphate,	Ferri Sulphas.
Exsiccated Ferrous Sulphate,	Ferri Sulphas Exsiccatus.
Granulated Ferrous Sulphate,	Ferri Sulphas Granulatus.
Mass of Ferrous Carbonate,	Massa Ferri Carbonatis.
Saccharated Ferrous Carbonate,	Ferri Carbonas Saccharatus.
Pills of Ferrous Carbonate,	Pilulæ Ferri Carbonatis.
Pills of Ferrous Iodide,	Pilulæ Ferri Iodidi.
Syrup of Ferrous Iodide,	Syrupus Ferri Iodidi.
Ferric Compounds.	
Ferric Chloride,	Ferri Chloridum.
Ferric Hydroxide with Magnesium Oxide,	Ferri Hydroxidum cum Magnesii Oxido.
Iron and Ammonium Citrate,	Ferri et Ammonii Citras.
Iron and Quinine Citrate,	Ferri et Quininæ Citras.
Ferric Phosphate,	Ferri Phosphas.
Solution of Ferric Chloride,	Liquor Ferri Chloridi.
Solution of Ferric Subsulphate,	Liquor Ferri Subsulphatis.
Solution of Ferric Sulphate,	Liquor Ferri Tersulphatis.
Solution of Iron and Ammonium Acetate,	Liquor Ferri et Ammonii Acetatis.
Tincture of Ferric Chloride,	Tinctura Ferri Chloridi.

Iron. Fe.—The kind of metallic iron recognized in the Pharmacopœia is that occurring in the form of soft, bright wire. It should be free from rust, and the commercial article, as it has usually been coated with grease or paraffin oil to protect it from moisture, must be thoroughly cleaned before it is used for pharmaceutical purposes. The kind of iron wire known in the trade as card-teeth, obtained as clippings and waste from the manufacturers of cotton cards, is usually preferred on account of its convenient form and general good quality; sometimes, however, card-teeth of a very inferior grade are sold, and require careful garbling and subsequent washing to remove grease and dirt.

Reduced Iron.—This preparation, also known as *Iron by Hydrogen* or *Quevenne's Iron*, represents more or less pure metallic iron in a state of fine division, obtained by reduction of ferric oxide with hydrogen gas. Ferric hydroxide is first dried, whereby it is changed to oxyhydrate, and then placed in an iron reduction tube so arranged that the same can be heated to dull redness, while a current of hydrogen gas, previously washed and dried by being passed through a moderately strong solution of potassium permanganate and afterward sulphuric acid, is constantly passed through it. The reducing action of hydrogen on ferric oxide may be illustrated by the following equation: $Fe_2O_3 + H_6 = Fe_2 + 3H_2O$. The supply of hydrogen is kept up as long as any oxygen is left, as shown by the escape of aqueous vapor from the tube. When reduction is complete, the tube and contents are allowed to cool slowly, while a slow stream of hydrogen is continued until the temperature has been reduced to that of the air; this is necessary, otherwise the hot, finely divided iron will be readily reoxidized by the air, as in that condition its avidity for oxygen is very marked.

The quantity of reduced iron depends, of course, upon the purity of the ferric hydroxide and the temperature employed. When ferric oxide is heated to 280° or 300° C. (536°–572° F.) in a stream of hydrogen, it is converted into ferroso-ferric oxide, Fe_3O_4, $3Fe_2O_3 + H_2 = 2Fe_3O_4$ or $2(FeO + Fe_2O_3) + H_2O$, but metallic reduction does not occur until a temperature of 400° C. (752° F.) and over is reached. A bright-red heat, however, is not employed, as it causes a dense, compact product, which is not desirable; therefore the commercial article, although a lighter powder, is usually contaminated with imperfectly reduced oxide.

Reduced iron should be free from lustre and of a grayish color, and when treated with warm diluted sulphuric or hydrochloric acid should leave not more than 1 per cent. of insoluble residue. Its value is based upon the proportion of metallic iron present; the U. S. and German Pharmacopœias both demand 90 per cent., while the British Pharmacopœia admits reduced iron of 75 per cent. purity. Frequent examinations of the commercial products have disclosed

the fact that inferior reduced iron is occasionally dispensed by pharmacists.

The Pharmacopœia directs that the purity percentage of reduced iron be determined by boiling a mixture of finely powdered mercuric chloride, reduced iron and distilled water for 5 minutes, cooling the mixture, filtering and titrating the filtrate with tenth-normal potassium permanganate solution. When mercuric chloride and reduced iron are digested together, the former is reduced to mercurous chloride with the formation of ferrous chloride, thus: $2HgCl_2 + Fe = FeCl_2 + 2HgCl$, showing that 1 atom, or 55.84 Gms., of metallic iron will react with 2 molecules, or 543.04 Gms., of mercuric chloride, forming 1 molecule, or 126.76 Gms., of ferrous chloride and 2 molecules, or 472.12 Gms., of mercurous chloride or calomel. The titration of the filtrate, after addition of sulphuric acid, with potassium permanganate solution takes place as follows: $10FeCl_2 + 2KMnO_4 + 8H_2SO_4 = 2Fe_2(SO_4)_3 + 6FeCl_3 + 2KCl + 2MnSO_4 + 8H_2O$, and shows that 10 molecules, or 1267.6 Gms., of ferrous chloride require 2 molecules, or 316.06 Gms., of potassium permanganate for complete oxidation and hence each mil. (or Cc.) of the tenth-normal solution consumed, containing 0.0031606 Gm. of potassium permanganate corresponds to 0.005584 Gm. of metallic iron. The number of mils. (or Cc.) of tenth-normal potassium permanganate solution consumed in the official assay, when multiplied by 0.5584 (0.005584×100) and divided by one-tenth of the weight of reduced iron originally taken (only one-tenth of the solution of ferrous chloride obtained being taken) will express the percentage of metallic iron in the sample.

Ferrous Sulphate. $FeSO_4 + 7H_2O$.—This salt, from which numerous other ferrous as well as ferric compounds are made, is obtained, for medicinal purposes, by acting on clean iron wire with diluted sulphuric acid, aiding the reaction with a little heat. The newly formed ferrous sulphate enters into solution and hydrogen gas is eliminated; thus, $Fe_2 + 2H_2SO_4 = 2FeSO_4 + H_4$. The salt is prone to oxidation if a strictly neutral solution be evaporated; hence a little free sulphuric acid is usually left in the liquid, which is then concentrated and crystallized.

The official ferrous sulphate contains 45.32 per cent. of water of crystallization, a portion of which is lost by efflorescence upon exposure to dry air; when exposed to moist air the salt undergoes oxidation, indicated by the formation of a brownish-yellow basic ferric sulphate. The crystals should therefore be preserved in well-stoppered bottles. The commercial crude ferrous sulphate, known as "copperas," is always more or less impure and not suited for pharmaceutical purposes.

The Pharmacopœia requires almost absolute purity for the official salt, namely that it shall contain not less than 54.36 per cent., nor more than 57.07 per cent. of anhydrous ferrous sulphate, corresponding to not less than 99.5 per cent. of the crystallized salt, which is deter-

mined by titration with tenth-normal potassium permanganate solution; each mil. (or Cc.) of the tenth-normal solution, containing 0.0031606 Gm. of potassium permanganate, must correspond to 0.027802 Gm. of the crystallized or 0.015191 Gm. of anhydrous ferrous sulphate. The number of mils. (or Cc.) of tenth-normal potassium permanganate solution consumed in the official assay, when multiplied by 1.5191 (0.015191 × 100) and divided by the weight of ferrous sulphate taken, will express the percentage of pure anhydrous ferrous sulphate in the sample. Each molecule of potassium permanganate is capable of converting 5 molecules of ferrous sulphate into ferric sulphate; thus $10(FeSO_4 + 7H_2O) + 2KMnO_4 + 8H_2SO_4 = 5Fe_2(SO_4)_3 + K_2SO_4 + 2MnSO_4 + 78H_2O$.

Exsiccated Ferrous Sulphate.—The Pharmacopœia directs exsiccated ferrous sulphate to be prepared by allowing the crystallized salt to effloresce in dry air at a temperature of about 40° C. (104° F.), and then exposing in a porcelain dish to the heat of a boiling waterbath, with constant stirring, until reduced to 64 or 65 per cent. of its original weight. This procedure does not render the salt anhydrous, for even at 115° C. (239° F.) 6.48 per cent. of water still remains, which requires a heat of nearly 300° C. (572° F.) for complete expulsion; at the latter temperature the ferrous sulphate is likely to undergo decomposition. The official preparation has approximately the composition $2FeSO_4 + 3H_2O$.

Dried ferrous sulphate may be conveniently employed for pill masses and other purposes, in place of the crystallized salt, in the proportion of 0.65 Gm. for 1 Gm. (or 6.5 grains for 10 grains) of the latter.

The Pharmacopœia requires that exsiccated ferrous sulphate shall contain not less than 80 per cent. of the anhydrous salt, which is determined exactly in the same manner as directed for the assay of crystallized ferrous sulphate, each mil. (or Cc.) of the tenth-normal potassium permanganate solution consumed corresponding to 0.015191 Gm. of pure anhydrous ferrous sulphate.

Granulated Ferrous Sulphate. $FeSO_4 + 7HO_2$.—This salt differs from official ferrous sulphate in being in the form of a crystalline powder instead of large crystals, containing, however, the same amount of water. It is of a much paler color than the crystals, and, owing to its mode of preparation, is less liable to oxidation. The addition of diluted sulphuric acid to the solution of ferrous sulphate prior to evaporation and granulation is intended to prevent oxidation, and washing of the crystalline powder with alcohol is for the purpose of removing the acid and uncombined water as completely as possible, thus facilitating drying. An equally efficient plan for making granulated ferrous sulphate is that of the German Pharmacopœia, which consists in filtering the acid solution of ferrous sulphate directly into

alcohol, whereby the salt is precipitated and can then be drained on a strainer and washed with diluted alcohol until free from acid. Rapid drying in direct sunlight is advantageous, as it prevents oxidation.

Granulated ferrous sulphate presents a convenient form for dispensing purposes.

Mass of Ferrous Carbonate, also known as *Vallet's Mass.*—The preparation of Vallet's Mass has been explained on page 426. The Pharmacopœia requires that it shall contain not less than 35 per cent. of ferrous carbonate, which is determined exactly in the same manner as directed for the assay of saccharated ferrous carbonate, by solution in diluted sulphuric acid and immediate titration with tenth-normal potassium dichromate solution. The reactions occurring are explained in detail under Saccharated Ferrous Carbonate.

Saccharated Ferrous Carbonate.—Although but little used at the present time, this preparation is still recognized in the Pharmacopœia. It closely resembles the preceding preparation except that it occurs in powder form, and is directed to contain a minimum limit of ferrous carbonate. The official directions are to pour a hot, slightly acidulated solution of 50 Gms. of ferrous sulphate into a warm solution of 35 Gms. of sodium bicarbonate contained in a flask, aiding decomposition by rotating the vessel. The precipitate is repeatedly washed with hot water until the newly formed sodium sulphate has been removed, after which the precipitate is drained, mixed with 10 Gms. of sugar of milk and 80 Gms. of sugar, evaporated to dryness, reduced to powder, and incorporated with sufficient sugar to make the finished product weigh 100 Gms. The reaction occurring between the ferrous sulphate and sodium bicarbonate may be seen from the following equation: $(FeSO_4 + 7H_2O) + 2NaHCO_3 = FeCO_3 + Na_2SO_4 + CO_2 + 8H_2O$. As the powder readily oxidizes if exposed to air, it must be preserved in tightly stoppered bottles.

The Pharmacopœia requires the presence of at least 15 per cent. of ferrous carbonate, determined by dissolving about 2 Gms. of the powder, accurately weighed, in diluted sulphuric acid and immediately titrating the solution with tenth-normal potassium dichromate solution. The reactions occurring involve first the conversion of he ferrous carbonate into ferrous sulphate, which is then oxidized and converted into ferric sulphate, as shown by the equation $6FeSO_4 + K_2Cr_2O_7 + 7H_2SO_4 = 3Fe_2(SO_4)_3 + K_2SO_4 + Cr_2(SO_4)_3 + 7H_2O$. Since 6 molecules, or 911.46 Gms., of anhydrous ferrous sulphate, representing 6 molecules, or 695.04 Gms., of ferrous carbonate, require 1 molecule, or 294.2 Gms., of potassium dichromate for complete oxidation, each mil. (or Cc.) of the tenth-normal solution, containing 0.0049033 Gm. of potassium dichromate, must correspond to 0.011584 Gm. of pure ferrous carbonate, for $294.2 : 695.04 : : 0.0049033 : x$ ($x = 0.011584$).

Syrup of Ferrous Iodide.—This preparation, as stated on page 272, is a saccharine solution of ferrous iodide, containing 5 per cent. of the latter compound. The first step in its manufacture is to obtain a solution of ferrous iodide by allowing iodine to act on an excess of metallic iron in the form of wire. The two elements combine in part, with the development of heat, forming some ferrous iodide which enables the remaining iodine to go into solution, and gradually all iodine is taken up by the iron, the color of the liquid changing to pale green. After heating the liquid to the boiling point, a small quantity of sugar is dissolved therein to prevent oxidation of the ferrous iodide solution and the liquid then filtered, the remaining iron wire and flask being rinsed with hot water, which is also passed through the filter. The balance of the sugar is then dissolved in the filtrate by means of heat. Syrup of ferrous iodide, if unprotected, readily becomes oxidized when in contact with air, as shown by the formation of a dark color on the surface, gradually spreading downward, and as this can be prevented by the presence of reducing agents, the Pharmacopœia directs that a small proportion of diluted hypophosphorous acid shall be added before the final weight of finished syrup is made up by addition of distilled water, which was first suggested by Judge in 1855, and has been found superior to all other preservatives proposed.

The Pharmacopœia requires that syrup of ferrous iodide shall contain not less than 4.75 per cent., nor more than 5.25 per cent. of pure ferrous iodide, which is determined by adding an excess of tenth-normal silver nitrate solution and some nitric acid to a definite weight of the syrup diluted with distilled water and heating the mixture until the precipitated silver iodide turns yellow; when cool, the excess of silver nitrate solution is titrated with tenth-normal potassium sulphocyanate solution, using ferric ammonium sulphate solution as indicator. The equation $2AgNO_3 + FeI_2 = 2AgI + Fe(NO_3)_2$ shows that 1 molecule, or 309.68 Gms., of ferrous iodide requires 2 molecules, or 339.78 Gms., of silver nitrate for complete precipitation, and hence 1 mil. (or Cc.) of the tenth-normal solution, containing 0.016989 Gm. of silver nitrate, must correspond to 0.015484 Gm. of ferrous iodide. Each Gm. of syrup of ferrous iodide must therefore require not less than 3.07 nor more than 3.4 mils. (or Cc.) of tenth-normal silver nitrate solution to conform to the pharmacopœial requirement.

Ferric Chloride.—The Pharmacopœia defines this compound to be a hydrated form of ferric chloride, corresponding to not less than 20 per cent. of metallic iron. It may be prepared by evaporating the official solution of ferric chloride on a waterbath to about 40 per cent. of its weight and then setting the liquid aside in a covered vessel to crystallize. The mass contains about 60 per cent. of anhydrous ferric chloride and may contain variable proportions of water, and since ferric chloride combines with different amounts of water under varying conditions, the Pharmacopœia gives no formula for the compound.

The salt occurs in pieces very deliquescent in moist air and is freely soluble in water and in alcohol; also soluble in glycerin and in ether. Upon exposure to light it is gradually reduced to the ferrous condition.

The Pharmacopœia requires that ferric chloride shall contain at least 20 per cent. of metallic iron in combination, which is determined volumetrically by allowing the ferric chloride to act upon potassium iodide and titrating the liberated iodine with sodium thiosulphate.

The equation $2FeCl_3 + 2KI = I_2 + 2FeCl_2 + 2KCl$ shows that the two salts decompose each other in molecular proportions, or 324.44 Gms., of ferric chloride, representing 111.68 Gms. of metallic iron, will react with 332.04 Gms. of potassium iodide, liberating 253.84 Gms. of iodine; hence each mil. (or Cc.) of tenth-normal sodium thiosulphate solution consumed in the official assay and representing 0.012692 Gm. of iodine must correspond to 0.005584 Gm. of metallic iron.

Ferric Hydroxide with Magnesium Oxide.—This preparation also known as Arsenic Antidote, consists of a mixture of ferric and magnesium hydroxides suspended in a dilute solution of magnesium sulphate, and is made by adding a dilute solution of ferric sulphate to a dilute mixture of calcined magnesia and water; the mixture is well shaken and is then ready for use.

The Pharmacopœia, with the view of economizing time in cases of emergency, recommends that the dilute solution of ferric sulphate and the mixture of magnesia and water be always kept on hand, ready for immediate use. The former consists of 40 mils. (or Cc.) of the official solution of ferric sulphate and 125 mils. (or Cc.) of water; the latter, of 10 Gms. of calcined magnesia added to 750 mils. (or Cc.) of water. In place of the 10 Gms. of calcium magnesia, 300 mils. (or Cc.) of magnesia magma may be used and diluted to 750 mils. (or Cc.) with water.

Ferric Phosphate.—This scale salt of iron, formerly officially designated as *soluble phosphate of iron*, must not be confounded with the insoluble commercial article known as Phosphate of Iron. The latter is a slate-colored powder of variable composition, consisting of a mixture of insoluble ferrous and ferric phosphates, obtained by precipitation of a solution of ferrous sulphate by means of sodium phosphate and drying the resulting product.

Ferric phosphate may be made by adding 11 parts of crystallized sodium phosphate to a solution of 10 parts of ferric citrate in twice its weight of water, evaporating the resulting green-colored solution, at a temperature not exceeding 60° C. (140° F.), to a syrupy consistence and spreading the same on glass plates,which are then placed in warm dust-proof drying closets so that a part of the moisture may evaporate and the product be obtained in the form of scales. Failure to obtain perfect scales may be due to insufficient concentration of the liquid before spreading it on glass, or to too high a temperature in drying.

It is important that uneffloresced sodium phosphate be used to avoid an excess of this salt, which would cause the scales to become opaque and white on standing. The salt should be preserved in tightly corked bottles, in a dark place, otherwise its color will gradually darken and its solubility be impaired.

The exact composition of this salt cannot be stated, as it may be a mixture of ferric phosphate and sodium citrate, or possibly a mixture of four salts, ferric and sodium phosphates and ferric and sodium citrates incomplete decomposition having taken place; hence the name sodio-citrophosphate of iron has been applied to the preparation.

The Pharmacopœia requires that ferric phosphate shall contain iron in combination corresponding to not less than 12 per cent. of that metal, which is determined by digesting a definite weight of the scale salt with hydrochloric acid and potassium iodide on a waterbath for 30 minutes at a temperature of 40° C. (104° F.), and then titrating the liberated iodine with tenth-normal sodium thiosulphate solution. The reactions involve the conversion of the iron salt into ferric chloride, which then decomposes the potassium iodide, as explained under Ferric Chloride on page 637. Each mil. (or Cc.) of the tenth-normal thiosulphate solution required corresponds to 0.005584 Gm. of metallic iron.

Although pyrophosphate of iron is no longer officially recognized, it is still used by physicians, and as it resembles ferric phosphate in appearance, the official test for distinguishing the two salts is important. Pyrophosphate of iron is not affected by the addition of magnesia mixture test-solution directed in the official test, whereas ferric phosphate will yield white ammonium magnesium phosphate, which when washed and treated with silver nitrate solution turns yellow.

Iron and Ammonium Citrate.—This preparation, also designated at times as soluble ferric citrate and ammonio-ferric citrate, is usually made by adding to a solution of ferric citrate, obtained by dissolving freshly prepared ferric hydroxide with the aid of citric acid, a slight excess of ammonia water, evaporating the liquid to a syrupy consistence at a temperature not exceeding 40° C. (104° F.) and then treating further as directed under Ferric Phosphate on page 637.

The Pharmacopœia requires that iron and ammonium citrate shall contain not less than 16 per cent. nor more than 18 per cent. of metallic iron in combination, which is determined by the iodometric method in exactly the same manner as directed for the assay of the iron in ferric phosphate on page 637.

Iron and ammonium citrate is more hygroscopic than ferric citrate, and upon exposure to air rapidly loses ammonia and becomes less soluble, hence it must be preserved in tightly stoppered bottles; light also has a deleterious effect upon it. If at any time the scale salt has suffered by age or careless exposure, ready solution can usually be effected by the cautious addition of a drop or two of ammonia water to the residue.

Iron and Quinine Citrate.—The reddish-brown scale salt, formerly official under this title, has been dropped from the Pharmacopœia and the name is now applied to the scale salt formerly known as Soluble Iron and Quinine Citrate. It is prepared by first dissolving quinine alkaloid in a solution of ferric citrate with addition of some citric acid, and then adding to this solution ammonia water cautiously as long as the precipitate formed is redissolved; an excess of ammonia must be carefully avoided. The color of the solution changes to greenish-yellow, and after concentration of the liquid to a syrupy consistence, it is spread on glass plate and allowed to scale, as explained under Ferric Phosphate. The scales are of a greenish, golden-yellow color, readily absorb moisture upon exposure to the air and are freely soluble in cold water.

The Pharmacopœia requires that iron and quinine citrate shall contain not less than 11.5 per cent. of anhydrous quinine and not less than 13 per cent. of metallic iron in combination. Both can be determined in one sample, the quinine gravimetrically and the iron by the iodometric method, and thus much time and labor saved. The official estimation of the quinine is easily accomplished; the addition of ammonia water to a solution of the salt precipitates the quinine as alkaloid, which, dissolving readily in the chloroform, can be withdrawn and the treatment with chloroform repeated twice, so as to insure the complete removal of the alkaloid. A globular separator (see Fig. 149, page 173) is better adapted for the operation than one of cylindrical shape, as by simple rotation the two liquids are brought into sufficiently intimate contact for abstraction of the alkaloid by the chloroform, and separation takes place rapidly; if shaking must be resorted to, it frequently happens that an emulsion results, which requires considerable time for separation. Owing to the low boiling point of chloroform (60° C. (140° F.)), the liquid should be evaporated with moderate heat only, so as to avoid loss by spurting, the residue being redissolved in a little alcohol and again evaporated to get rid of all traces of chloroform and afterward dried at 100° C. (212° F.) to constant weight.

The residuary aqueous liquid retains all the ferric citrate, and, after removal of all the chloroform and ammonia by heating on a waterbath it is diluted with water and digested in a glass-stoppered bottle with hydrochloric acid and potassium iodide for 30 minutes, the liberated iodine being subsequently titrated with tenth-normal sodium thiosulphate solution. The details of this assay are fully explained under Ferric Phosphate on page 637.

Solution of Ferric Chloride.—An aqueous solution of ferric chloride, $FeCl_3$, containing an amount of ferric chloride corresponding to not less than 10 per cent., nor more than 11 per cent. of metallic iron. The official directions for preparing this solution consist in treating bright iron wire with hydrochloric acid diluted with about one-half

its weight of water, oxidizing the resulting solution by means of nitric and hydrochloric acids, and finally, after addition of a little more hydrochloric acid, bringing the liquid to a definite weight by addition of distilled water.

The mixture of iron, hydrochloric acid, and water is heated on a waterbath for not less than 1¼ hours or until effervescence ceases, which latter is due to the escape of hydrogen, the ferrous chloride formed dissolving in the water, as illustrated by the equation $Fe_2 + 4HCl = 2FeCl_2 + H_4$. Not all the iron is dissolved, an excess being purposely used to facilitate the reaction. The mixture is then boiled and filtered through paper, the flask and wire being rinsed with hot water. A further addition of hydrochloric acid is at once made to the filtrate, to avoid the formation and deposit of ferric oxychloride, as the ferrous chloride is readily oxidized by the air.

The liquid, which has now assumed a deep green color, is poured slowly into a porcelain dish containing nitric acid, and then warmed. A change in color to reddish-brown at once occurs, owing to the conversion of the ferrous into ferric chloride, accompanied by effervescence and escape of red fumes, which may be illustrated by the following equation: $3FeCl_2 + 3HCl + HNO_3 = 3FeCl_3 + NO + 2H_2O$. The red fumes are due to nitrogen dioxide, NO_2 or N_2O_4, resulting from a union of nitric oxide, NO, with some of the oxygen of the air.

It frequently happens that the color of the liquid remains blackish for some time; this is due either to a union of ferrous chloride with nitric oxide, in which case it disappears upon further heating as oxidation progresses, or, it may be, to an insufficiency of nitric acid and consequent imperfect oxidation.

To remove all nitrogen compounds, the liquid is heated on a sandbath until free from nitrous odor, after which it is tested for ferrous salt, as prescribed: and if more nitric acid is necessary, this should be added drop by drop to the hot liquid and only as long as effervescence results, as an excess of nitric acid is not readily removed. If ferrous salt is found absent, a test for nitric acid should be made, and, if present, the liquid must be boiled on a sandbath until entirely free therefrom; this is preferably done with careful addition of small quantities of hydrochloric acid, which facilitates the expulsion of nitric acid by decomposing it, and prevents the formation of oxychloride. Should the liquid, upon boiling to free it from nitric acid, separate a blackish-brown deposit on the sides or bottom of the dish, this would indicate ferric oxychloride, which can only be overcome by careful addition of hydrochloric acid to the hot liquor until a 0.5 per cent. solution of the latter in water remains clear upon boiling and cooling.

The final addition of hydrochloric acid to the liquid is for the purpose of preventing the formation of ferric oxychloride by having an excess of the acid present.

Solution of ferric chloride contains a small amount of free hydrochloric acid, but should be absolutely free from ferrous salt and ferric oxychloride, as well as nitric acid and other nitrogen compounds. Commercial solutions of ferric chloride are sometimes contaminated with ferric oxychloride, and nitrous odors are occasionally perceptible.

The official solution has a specific gravity of from 1.29 to 1.32 at 25° C. (77° F.), and contains about 0.3785 Gm. of anhydrous ferric chloride in each mil. (or Cc.); its chief use in pharmacy is for the preparation of the tincture of ferric chloride.

The Pharmacopœia requires that the official solution shall contain an amount of ferric chloride corresponding to not less than 10 per cent., nor more than 11 per cent. of metallic iron, and that the amount of chlorine present, as free hydrochloric acid, shall not be less than 3 per cent., nor more than 5 per cent., in excess of that required to combine with the iron present as ferric chloride. The determination of the metallic iron content is made in the same manner as explained under Ferric Chloride on page 637, and the total amount of chlorine present is determined in the usual manner by precipitation with tenth-normal silver nitrate solution in the presence of nitric acid, each mil. (or Cc.) of the silver solution consumed corresponding to 0.003546 Gm. of chlorine. As each Gm. of metallic iron combines with 1.905 Gms. of chlorine to form ferric chloride, the percentage of metallic iron found, when multiplied by 1.9, will express the percentage of chlorine combined as ferric chloride, and if this percentage of chlorine be subtracted from the total percentage of chlorine determined by titration with silver solution, as stated above, the remainder will express the percentage of chlorine present as free hydrochloric acid.

Solution of Ferric Subsulphate.—An aqueous solution of basic ferric sulphate of variable composition. It is prepared by adding 675 Gms. of crystallized ferrous sulphate to a heated mixture of 65 Gms. of sulphuric and 70 Gms. of nitric acid, and 500 mils. (or Cc.) of water; when effervescence ceases the liquid is tested for ferrous salt, and, if this be found present, nitric acid is added drop by drop to the hot liquid as long as it causes effervescence and the disengagement of red fumes. Finally the liquid is boiled until a clear ruby-red solution is obtained entirely free from nitrous odor, and is diluted with water to the weight of 1000 Gms.

The ferrous sulphate is used in the form of a coarse powder, and added to the hot acid mixture in divided portions, in order to avoid a violent reaction. In the presence of nitric and sulphuric acids oxidation takes place, converting the ferrous into a ferric salt, but, owing to an insufficient amount of sulphuric acid, a basic, instead of a normal, ferric sulphate is produced, the composition of which is variable; hence no definite formula can be assigned to it, although the following, $Fe_4O(SO_4)_5$, is used by some to illustrate the nature of the salt. In the preparation of this, as well as the next following

solution, copious red vapors are evolved, due to the escape of nitric oxide in the air, and the liquid assumes a black tint temporarily, on account of a union between the ferrous sulphate and nitric oxide; these phenomena have been explained in connection with the manufacture of solution of ferric chloride (p. 640).

If a little sulphuric acid be added to solution of ferric subsulphate, the color becomes lighter, and, if added to the extent of one-half the volume of the latter, a white mass, consisting of anhydrous ferric sulphate, will separate.

The name Monsel's Solution is usually applied to this preparation, which is also prescribed by physicians as solution of persulphate of iron; although chemically incorrect, this last name is sometimes employed in this country when the official solution of the subsulphate is intended, particularly by some of the older physicians.

Solution of ferric subsulphate is a dense solution, having a specific gravity of about 1.548 at 25° C. (77° F.), and is apt to separate a semisolid crystalline whitish mass upon standing, particularly in the cold. This is not a sign of deterioration, but is due to the concentration of the solution, and can be overcome by placing the bottle in warm water for a while and agitating, when perfect solution will be restored. The Pharmacopœia demands that the amount of basic ferric sulphate present in this solution shall correspond to not less than 13 per cent. nor more than 14 per cent. of metallic iron, to be determined by the iodometric method in the same manner as directed for the other iron solutions.

Solution of Ferric Sulphate.—An aqueous solution of normal ferric sulphate, $Fe_2(SO_4)_3$, containing about 36 per cent. of the salt. This solution is not used medicinally, being employed only for the preparation of other iron compounds. It is made in the same manner as solution of ferric subsulphate, except that a larger proportion of acids is used, a different product being, therefore, obtained. The following equation, $6(FeSO_4 + 7H_2O) + 3H_2SO_4 + 2HNO_3 = 3Fe_2(SO_4)_3 + 2NO + 46H_2O$, shows that the reaction results in the formation of a normal salt, which is the chief point of difference in the composition of this and the preceding solution.

Solution of ferric sulphate is known in the British Pharmacopœia as Solution of Persulphate of Iron, but the official Latin title of the United States Pharmacopœia, Liquor Ferri Tersulphatis, is preferable, as at once indicating the true nature of the chemical compound present. It can readily be distinguished from Monsel's Solution by a lower density and lighter color, and also by not separating white ferric sulphate upon addition of one-half its volume of sulphuric acid. The solution has a specific gravity of about 1.432 at 25° C. (77° F.), and is required to contain an amount of ferric sulphate corresponding to not less than 10 per cent. nor more than 11 per cent. of metallic iron.

Solution of Iron and Ammonium Acetate.—This well known preparation is usually prescribed by physicians as "Basham's Mixture," or under its old official (Pharmacopœia, 1880) title, Mistura Ferri et Ammonii Acetatis. It is readily prepared by adding to solution of ammonium acetate successively diluted acetic acid, tincture of ferric chloride, aromatic elixir, glycerin, and sufficient water to bring the total volume up to the required quantity.

As its name indicates, the solution contains both iron and ammonium acetates, the former salt, to which the deep red color of the liquid is due, being formed, at the time of preparation, by mutual decomposition between the ferric chloride and a part of the ammonium acetate; a small amount of ammonium chloride also is formed, It is important that the solution of ammonium acetate be not alkaline, so that, upon addition of the diluted acetic acid, an excess of the latter shall be present, to avoid the formation of basic ferric acetate when the tincture of ferric chloride is added.

If made strictly according to the formula of the Pharmacopœia, this preparation will deposit upon standing for some time, especially in hot weather, but this can be prevented by doubling the quantity of glycerin directed; when so made the solution has been found to remain perfectly clear for 2 years. Even increasing the quantity of glycerin to 200 mils. (or Cc.) in the official formula has kept the solution clear for over 6 months; hence it is not necessary to make it fresh whenever wanted.

Tincture of Ferric Chloride.—This is a hydro-alcoholic solution of ferric chloride, containing about 13 per cent. of the anhydrous salt. The Pharmacopœia directs that 350 mils. (or Cc.) of solution of ferric chloride shall be mixed with sufficient alcohol to yield 1000 mils. (or Cc.); this will require slightly more than 650 mils. (or Cc.) of alcohol, on account of the contraction of volume which invariably results when aqueous liquids and alcohol are mixed. The official directions, to set the mixture aside in an amber-colored bottle for a period of three months, are for the purpose of allowing certain changes to take place before dispensing the tincture; these changes are due to reaction between the acid solution of ferric chloride and alcohol, resulting in the formation of ethyl chloride and other ethereal products, which modify the odor of the preparation to some extent, and are said also to possess marked medicinal properties. By some authorities it is claimed that these changes will not be completed at the end of three months, and that, in fact, they will continue for a period of six or nine months.

Occasionally the mixture is found to deposit a yellowish-brown sediment; this is due to ferric oxychloride present in the solution of ferric chloride used, and is an evidence that the latter preparation was not properly made. Upon exposure to sunlight tincture of ferric chloride is gradually changed in color, assuming a greenish-brown tint,

owing to reduction of the ferric to ferrous salt; hence it should be protected from light.

The proportion of ferric chloride present in the official tincture should correspond to not less than 4.48 per cent. of metallic iron, and is determined in the usual manner with potassium iodide, and sodium thiosulphate. In order to insure the absence of ferrous salt and other impurities in the official test, the Pharmacopœia directs that about 5 mils. (or Cc.) of the tincture, accurately weighed, be evaporated to dryness on a waterbath, mixed with 2 mils. (or Cc.) of hydrochloric acid and 5 mils. (or Cc.) of hydrogen dioxide solution and again evaporated to dryness before it is dissolved in water, and further treated with hydrochloric acid and potassium iodide. Each mil. (or Cc.) of tenth-normal sodium thiosulphate solution required for the liberated iodine corresponds to 0.005584 Gm. of metallic iron, and each Gm. of tincture of ferric chloride, if of official strength should require not less than 8 mils. (or Cc.) of the tenth-normal thiosulphate solution, in the official assay. The details of the reactions are explained under Ferric Chloride on page 637.

Besides the official preparations of iron, the following are occasionally employed:

Benzoate of Iron. Ferric Benzoate. $Fe(C_7H_5O_2)_3$ **or** $(C_6H_5COO)_3Fe$.—This salt may be obtained as a pale-brownish powder by adding a concentrated solution of sodium benzoate to a solution of ferric sulphate, washing the resulting precipitate with a little cold water, and drying the same.

Dialyzed Iron.—Under this name a solution of a highly basic ferric oxychloride has been used by physicians for many years. It is recognized in the *National Formulary* by the name Liquor Ferri Oxychloridi, and in the German Pharmacopœia as Liquor Ferri Oxychlorati Dialysati. The former authority does not direct that the solution of oxychloride of iron obtained by direct solution of freshly prepared ferric hydroxide in very weak hydrochloric acid, be dialyzed, and also adds glycerin to the solution, to the extent of 12.5 per cent. by volume. The German Pharmacopœia on the other hand does direct that ammonia water be gradually added to a solution of ferric chloride as long as the precipitate formed is redissolved, after which the mixture is stirred until a clear solution results, which is then dialyzed, the dialysate being finally concentrated by evaporation with the aid of gentle heat until the liquid has a specific gravity of from 1.043 to 1.047. The latter preparation must contain iron in combination corresponding to 3.3 to 3.6 per cent. of metallic iron.

Glycerophosphate of Iron. Ferric Glycerophosphate. $Fe_2(C_3H_5(OH)_2PO_4)_3$.—This salt may be obtained by dissolving freshly pre-

cipitated and well-washed ferric hydroxide in an aqueous solution of glycerophosphoric acid, evaporating the solution in a vacuum apparatus to a syrupy consistence, and then spreading on plates of glass and drying at a gentle heat. It forms yellow scales, soluble in water and diluted alcohol.

Iodide of Iron. Ferrous Iodide. FeI_2.—This preparation is obtained by first making a solution of ferrous iodide, by direct union of iodine and iron in the presence of water, and evaporating the pale-green solution to dryness in a bright iron dish. It occurs as a very deliquescent black mass, which must be carefully preserved in a tightly stoppered bottle.

Lactate of Iron. Ferrous Lactate. $Fe(C_3H_5O_3)_2 + 3H_2O$ or $(CH_2CHOHCOO)_2Fe + 3H_2O$.—This salt may be prepared by double decomposition between solutions of calcium lactate and ferrous sulphate, the newly formed calcium sulphate being completely removed by addition of alcohol; the filtrate is finally evaporated and crystallized. It may also be obtained by digesting pure iron wire with diluted lactic acid until reaction ceases, then filtering, concentrating, and crystallizing the solution. In the first process the reaction is as follows: $Ca(C_3H_5O_3)_2.5H_2O + FeSO_4.7H_2O = Fe(C_3H_5O_3)_2 + CaSO_4 + 12H_2O$; while in the second process ferrous lactate is formed with elimination of hydrogen; thus, $Fe_2 + 4HC_3H_5O_3 = 2Fe(C_3H_5O_3)_2 + H_4$.

Two varieties of ferrous lactate occur in commerce, one in well defined crystalline crusts and another in the form of a crystalline powder. The first-named is to be preferred for pharmaceutical purposes; it is, as a rule, more soluble and less likely to have become oxidized. Ferrous lactate should be preserved in tightly stoppered bottles, in a dry place, as upon exposure to moist air it is gradually converted into a ferric salt.

Malate of Iron.—Impure ferrous malate occurs in the form of a blackish-green mass, obtained by digesting the juice of sour apples with iron filings, filtering, and evaporating the solution to the consistence of an extract. It is recognized in the *National Formulary* under the name of Extractum Ferri Pomatum.

Saccharated Oxide of Iron.—This preparation, known also as soluble oxide of iron, is officially recognized in the German Pharmacopœia, and is used to some extent in this country. It is obtained by adding to freshly prepared ferric hydroxide a given proportion of sodium hydroxide solution and sugar, heating the mixture to perfect solution, then evaporating to dryness, powdering, and incorporating with it sufficient sugar to bring the product up to a definite weight, representing the equivalent of 3 per cent. of metallic iron. The exact composition of the reddish-brown powder is as yet not clearly under-

stood; it is considered to be a sodio-ferric saccharate, the presence of the alkali being essential, as, with sugar alone, ferric hydroxide does not form a perfectly soluble compound.

Salicylate of Iron. Ferrous Salicylate. $Fe(C_7H_5O_3)_2$ **or** $(C_6H_4(OH)COO)_2Fe$.—This is best prepared by dissolving freshly precipitated ferrous carbonate in water by means of salicylic acid, with the aid of gentle heat, filtering, and evaporating the solution to dryness on a waterbath.

Valerate of Iron. Ferric Valerate.—This salt, at one time officially recognized as ferric valerianate, is best obtained by double decomposition between cold solutions of ferric sulphate and sodium valerate, washing the resulting precipitate with a little cold water, and drying at a moderate temperature. The composition of ferric valerate is variable, depending upon the care employed in washing the precipitate and the temperature at which it is dried. The normal salt would have the composition $Fe(C_5H_9O_2)_3$, but the commercial product is mixed often with basic salt, as shown by its increased yield of ferric oxide upon ignition.

Ferric valerate is rarely used in other than pill form, although it is readily soluble in alcohol.

Solution of Albuminate of Iron.—An aromatic solution of ferric albuminate prepared, according to the *National Formulary* by adding solution of ferric oxychloride to an aqueous solution of fresh egg albumen, allowing the mixture to stand for 2 hours, then adding a solution of sodium citrate, and when perfect solution has been effected adding aromatic elixir, alcohol and sufficient distilled water to make up the required volume.

Syrup of Soluble Oxide of Iron.—This syrup may be conveniently prepared extemporaneously as wanted, by forming a solution of equal parts by weight of saccharated oxide of iron, water, and simple syrup. This is the formula suggested as an alternative in the *National Formulary;* a more tedious process for making the syrup from solution of ferric chloride is also given by the same authority. Each fluidounce of the syrup represents about $6\frac{1}{2}$ grains of metallic iron, or about 0.0143 Gm. in each mil. (or Cc.).

Tincture of Citro-chloride of Iron.—The *National Formulary* directs this preparation, which is also known as "tasteless tincture of iron," to be made by adding sodium citrate to a diluted solution of ferric chloride and heating until perfect solution is effected. Alcohol is then added, and finally sufficient water to make up the required volume. The tincture is of a deep-green color, and the amount of iron represented is about the same as in the official tincture of ferric chloride.

CHAPTER XLIX.

THE COMPOUNDS OF MANGANESE AND CHROMIUM.

Of these two metals the Pharmacopœia recognizes but 2 compounds, and even these are not frequently employed. The official preparations are as follows:

Official English name.	Official Latin name.
Precipitated Manganese Dioxide,	Mangani Dioxidum Præcipitatum.
Chromium Trioxide,	Chromii Trioxidum.

Precipitated Manganese Dioxide.—This compound consists chiefly of manganese dioxide with small amounts of other oxides of manganese. Being obtained by precipitation, it is free from foreign matter and therefore well suited for internal use. Its preparation involves the precipitation of manganous hydroxide from a solution of the sulphate by addition of ammonia water, and its conversion into manganic hydroxide by means of hydrogen dioxide, which is then dried at 150° C. (302° F.) and changed to manganese dioxide, the water of hydration being nearly all driven off at that temperature. The following equations indicate the successive steps in the manufacture: $MnSO_4 + 2NH_4OH = Mn(OH)_2 + (NH_4)_2SO_4$; $Mn(OH)_2 + H_2O_2 = Mn(OH)_4$ or $MnO_2 + 2H_2O$. It is a very fine black powder, which, when heated to redness, gives off oxygen and is converted into manganoso-manganic oxide Mn_3O_4.

The Pharmacopœia requires that precipitated manganese dioxide shall contain not less than 80 per cent. of pure MnO_2, but some manufacturers are offering an article of over 90 per cent. purity. The determination is made volumetrically with oxalic acid. In the official test an excess of tenth-normal oxalic acid solution is added to a definite weight of precipitated manganese dioxide and after addition of some sulphuric acid the mixture is heated to 80° C. (176° F.) on a waterbath; the excess of oxalic acid is then titrated with tenth-normal potassium permanganate solution. The equation $MnO_2 + (H_2C_2O_4 + 2H_2O) + H_2SO_4 = 2CO_2 + MnSO_4 + 4H_2O$ shows that 1 molecule, or 86.93 Gms., of manganese dioxide is capable of oxidizing 1 molecule, or 126.05 Gms., of crystallized oxalic acid, and hence each mil. (or Cc.) of the tenth-normal acid solution represents 0.0043465 Gm. of pure MnO_2. The number of mils. (or Cc.) of tenth-normal oxalic acid solution consumed by the precipitated manganese dioxide in the official assay, when multiplied by 0.43465 (0.0043465 × 100) and divided by the weight of the sample taken, will express the percentage of pure MnO_2 present.

Commercial native manganese dioxide, also known as black oxide of manganese, or pyrolusite, is no longer recognized officially. It is found in different parts of Russia, Germany, France, Spain, and Great Britain, and also in Nova Scotia, Vermont, Pennsylvania, and other parts of North America. Sometimes it is found nearly pure, but is generally associated with other manganic ores, particularly with the inferior brown manganite, and often with iron, lime, baryta, silica, .etc. Pyrolusite is the most important and most abundant manganese mineral. When pure it consists of 63.19 per cent. of manganese and 36.81 per cent. of oxygen. The only use to which black oxide of manganese is put in pharmacy is in the preparation of pure chlorine water, and for this purpose it should contain at least 65–70 per cent. of manganese dioxide.

Chromium Trioxide. Chromic Anhydride. CrO_3.—This compound, formerly recognized in the Pharmacopœia as chromic acid, and still commercially better known by that name, may be obtained by allowing strong sulphuric acid to act on a cold saturated solution of potassium dichromate, chromium trioxide being set free, as shown by the following equation: $K_2Cr_2O_7 + 2H_2SO_4 = 2CrO_3 + 2KHSO_4 + H_2O$: this is due to the fact that chromic acid proper, H_2CrO_4, like arsenous and carbonic acids, can exist only in solution, and upon evaporation of the latter is at once converted into its anhydride. The mixture becomes heated, and upon cooling separates needle-shaped crystals, which are drained and dried upon porous tiles. When prepared by the ordinary methods chromium trioxide is usually contaminated with sulphuric acid and potassium salts, the former rendering it very hygroscopic. Inasmuch as the Pharmacopœia demands the absence of sulphuric acid, the process of manufacture is probably modified by washing the crystals dried on porous plates with small quantities of strong nitric acid, again drying on plates, and finally heating to 60°–80° C. (140°–176° F.) in order to remove adhering nitric acid. The color of commercial chromium trioxide is not uniform, depending upon the purity of the article; if pure, the proper color is dark purplish-red, while a light scarlet-red color usually indicates the presence of sulphuric acid.

The Pharmacopœia requires that the official chromium trioxide shall contain not less than 95 per cent. of pure CrO_3, to be determined by the iodometric method by adding to a solution of 0.15 Gm. of the compound 3 mils. (or Cc.) of hydrochloric acid and about 2 Gms. of potassium iodide, and then titrating the liberated iodine with tenth-normal sodium thiosulphate solution, using starch test-solution as an indicator. The operation is considered completed when the deep blue color of iodized starch has been changed to a light green. The reactions involved in this test may be illustrated by the following equations, the first step being the conversion of chromium trioxide into chromic acid by solution of the former in water: $CrO_3 + H_2O =$

H_2CrO_4; $2H_2CrO_4 + 6HCl = 2CrCl_3 + O_3 + 5H_2O$; $6KI + 6HCl = 6KCl + 6HI$; $6HI + O_3 = I_6 + 3H_2O$; showing that for every molecule, or 100 Gms., of pure CrO_3 present 3 atoms, or 380.76 Gms., of iodine will be liberated; hence each mil. (or Cc.) of the tenth-normal sodium thiosulphate solution consumed and corresponding to 0.012692 Gm. of iodine, must also correspond to 0.003333 Gm. of pure CrO_3.

Owing to its ready decomposition by organic substances, often with explosive violence, chromic anhydride should never be brought into contact with alcohol or glycerin, and should always be weighed on watch glasses, never on paper; if its aqueous solution requires filtration this must be done by means of asbestos or glass wool.

CHAPTER L.

THE COMPOUNDS OF MERCURY.

NEXT to the preparations of iron, those of mercury are the most important obtained from the heavy metals. Like the iron compounds, they are divided into two series, designated as mercurous and mercuric compounds, respectively. In mercurous compounds, mercury appears univalent, while in mercuric compounds it acts like a bivalent element. The Pharmacopœia recognizes metallic mercury and 16 preparations and compounds of it as shown by the following list:

Official English name.	Official Latin name.
Mercury,	Hydrargyrum.
Mercury with Chalk,	Hydrargyrum cum Creta.
Ammoniated Mercury,	Hydrargyrum Ammoniatum.
Mild Mercurous Chloride,	Hydrargyri Chloridum Mite.
Yellow Mercurous Iodide,	Hydrargyri Iodidum Flavum.
Corrosive Mercuric Chloride,	Hydrargyri Chloridum Corrosivum.
Red Mercuric Iodide,	Hydrargyri Iodidum Rubrum.
Yellow Mercuric Oxide,	Hydrargyri Oxidum Flavum.
Red Mercuric Oxide,	Hydrargyri Oxidum Rubrum.
Mass of Mercury,	Mass Hydrargyri.
Mercurial Ointment,	Unguentum Hydrargyri.
Diluted Mercurial Ointment,	Unguentum Hydrargyri Dilutum.
Ointment of Ammoniated Mercury,	Unguentum Hydrargyri Ammoniati.
Ointment of Mercuric Nitrate,	Unguentum Hydrargyri Nitratis.
Ointment of Yellow Mercuric Oxide,	Unguentum Hydrargyri Oxidi Flavi.
Mercuric Oleate,	Oleatum Hydrargyri.
Poison Tablets of Corrosive Mercuric Chloride,	Toxitabellæ Hydrargyri Chloridi Corrosivi.

Mercury. Hg.—Nearly all commercial mercury is obtained by roasting the ore known as cinnabar, crude native sulphide of mercury, the sulphur escaping as sulphur dioxide, while metallic mercury is condensed and collected in suitable apparatus. As thus obtained, it is usually contaminated with lead, copper, and other metals, from which it is freed by treatment with diluted nitric acid; it is finally washed with water and dried. On a small scale mercury may readily be purified by shaking with solution of ferric chloride and subsequently washing with water. For medicinal purposes, only pure redistilled mercury, which possesses a bright luster, should be used; if contaminated with dust or other mechanical impurities, mercury may be successfully strained through a piece of close muslin or chamois skin. For weighing small quantities of mercury, it is most conveniently transferred from the stock bottle to the balance by means of a dropping tube or pipette, as owing to its great cohesiveness it cannot be poured readily from a bottle.

The Pharmacopœia requires 99.5 per cent. purity for metallic mercury and directs that this be determined by dissolving a definite weight of mercury in diluted nitric acid and titrating the resulting solution of mercuric nitrate with tenth-normal potassium sulphocyanate solution. The equations $Hg + 4HNO_3 = Hg(NO_3)_2 + 2NO_2 + 2H_2O$ and $Hg(NO_3)_2 + 2KCNS = Hg(CNS)_2 + 2KNO_3$ show that 1 molecule, or 324.62 Gms., of mercuric nitrate, containing 1 atom, or 200.6 Gms., of metallic mercury, requires 2 molecules, or 194.36 Gms., of potassium sulphocyanate for complete decomposition, and hence each mil. (or Cc.) of the tenth-normal solution consumed in the official test before production of a permanent red color, and containing 0.009718 Gm. of potassium sulphocyanate, must correspond to 0.01003 Gm. of metallic mercury.

Mercury may also be assayed electrolytically by dissolving a definite small quantity, accurately weighed, in diluted nitric acid and transferring the solution to a previously weighed mercury cathode cup consisting of a glass cylinder about 6.5 cm. high and 3.5 cm. in diameter, into which is fused a platinum wire near the bottom, and containing 50 to 60 Gms. of pure mercury, the platinum wire being in contact with the mercury; as an anode, a platinum spiral is used, to which must be attached a contrivance for rotating the anode. A current of 1.5 to 2 amperes and 7 to 10 volts is then passed through the solution, at the same time rotating the anode from 500 to 600 revolutions per minute.

After 20 minutes, when the mercury has all been removed from the solution (to be ascertained by removing a few drops of the solution and testing with hydrogen sulphide), wash the mercury with distilled water with the aid of a siphon and without interrupting the current until the latter drops to zero. The cathode cup is then removed, the mercury washed with alcohol, followed by ether, removing most of the remaining ether with filter paper, then dried in a desiccator over sulphuric acid and weighed. Having ascertained the increase of weight of the mercury in the cup, multiply the same by 100 and divide the product by the weight of mercury originally taken for the assay; the quotient will express the percentage of pure mercury in the sample.

Mercury with Chalk.—Although not so much used as formerly, this preparation, known also as "Gray Powder," is still a very important one, as it represents mercury in a state of fine division in powder form, and is frequently used in infantile disorders. The official method of preparation depends upon the extinguishment of the mercury by means of succussion, 38 Gms. of mercury being shaken with 10 Gms. of clarified honey, for ten hours or longer in a strong bottle; this is best effected in a mechanical shaker, attached to a water motor or an electric motor. The mixture of mercury and honey is afterward added to a thick, creamy paste, made of 57 Gms. of prepared chalk and a sufficient quantity of water, the whole being triturated until a

uniform mixture results, which is finally dried at the ordinary temperature, and should be reduced to powder without trituration.

In this state of fine division mercury is very prone to oxidation if exposed to air and light; hence the powder should be kept well protected from both. While traces of mercurous oxide cannot be entirely avoided, the presence of mercuric oxide should be carefully guarded against, and any change in color from gray to pink or reddish, indicating dangerous oxidation, renders the article unfit for use; neither should mercury with chalk be dispensed if the color has turned very dark gray or blackish, as this shows excessive mercurous oxidation. In the official test, mercurous oxide is detected by precipitation, as calomel by hydrochloric acid, while the mercuric oxide is converted into mercuric chloride, and is then precipitated either as mercuric sulphide by hydrogen sulphide, or as calomel (being afterward reduced to metallic mercury) by stannous chloride.

The Pharmacopœia requires that mercury with chalk shall contain not less than 37 per cent., nor more than 39 per cent. of metallic mercury, which may be determined both volumetrically and electrolytically exactly in the same manner as directed for the assay of mercury given above.

Ammoniated Mercury.—NH_2HgCl.—This compound, also known as *white precipitate*, may be obtained by pouring a solution of mercuric chloride slowly, with constant stirring, into ammonia water, when the following reaction occurs: $HgCl_2 + 2NH_4OH = NH_2HgCl + NH_4Cl + 2H_2O$. Both liquids are used cold, and the resulting precipitate is washed with a small quantity of cold water to which some ammonia water has been added. Finally, the precipitate is dried in a dark place at a temperature not exceeding 30° C. (86° F.). These directions are for the purpose of avoiding the formation of a basic yellow compound, $NH_2(Hg_2O)Cl$, which is likely to occur on exposure to light or heat, and even excessive washing with plain water.

The constitution of ammoniated mercury may be explained in two different ways. The simplest way is to consider it as mercuric chloride in which an atom of chlorine has been replaced by the amido group NH_2, and in that case the name mercuric chloramide will be appropriate; the other view is that the compound is derived from ammonium chloride by replacement of two hydrogen atoms by a bivalent atom of mercury, as suggested by the name mercuric ammonium chloride. Ammoniated mercury is known also as amido-chloride of mercury, and is sometimes prescribed by German physicians as *hydrargyrum amidato-bichloratum*.

The Pharmacopœia requires that ammoniated mercury shall contain an amount of mercurammonium chloride corresponding to not less than 78 per cent., nor more than 80 per cent. of metallic mercury, which may be determined gravimetrically as mercuric sulphide, by dissolving an accurately weighed portion of ammoniated mercury in a

mixture of hydrochloric acid and water with the aid of a gentle heat, diluting the solution and passing hydrogen sulphide through the cold solution until saturated and the precipitate of mercuric sulphide subsides, leaving the supernatant liquid clear. Collect the precipitate on counterpoised filters, wash it well with cold distilled water and finally with three portions of about 10 mils. (or Cc.) each of alcohol. Then close the tip of the funnel with a cork stopper, add sufficient carbon tetrachloride to cover the precipitate, cover the funnel with a watch glass, and allow it to stand for about 30 minutes. Then drain off the solvent and wash the precipitate with further portions of carbon tetrachloride until after evaporating about 1 mil. (or Cc.) of the filtrate no visible residue remains. Remove the adhering carbon tetrachloride by washing with several small portions, about 10 mils. (or Cc.) each, of alcohol and after drying in the air, transfer to an oven and dry to constant weight at about 110° C. (230° F.). Since 1 Gm. of ammoniated mercury is capable of producing 0.9229+ Gm. of mercuric sulphide and each Gm. of mercuric sulphide represents 0.862+ Gm. of metallic mercury, not less than 0.90487 Gm., nor more than 0.92807 Gm. of mercuric sulphide should be obtained from 1 Gm. of ammoniated mercury to show the purity demanded by the Pharmacopœia.

Ammoniated mercury may also be assayed electrolytically as follows: About 0.5–0.6 Gm. of the compound, accurately weighed is introducted into a mercury cathode cup (see under Mercury) previously weighed and 10 mils. (or Cc.) of a strong solution of crystallized sodium sulphide (50 Gms. in 100 mils.) is added and the mixture agitated to effect solution as far as possible. After dilution with distilled water to about 30 mils. (or Cc.), a current of 2–3 amperes and 7–10 volts is passed through the solution for 30 minutes (or until a few drops of the liquid do not give a black precipitate or coloration when gently warmed with a few drops of concentrated ammonium chloride solution), rotating the anode about 500 revolutions per minute. Before washing with alcohol, as directed under Mercury, the mercury is allowed to stand with some weak acetic acid (2–3 per cent.) until bubbles cease to be evolved. After washing with alcohol and ether and drying as in the case of metallic mercury, the increase of weight is easily determined and from this the percentage of metallic mercury in the sample readily calculated.

Mild Mercurous Chloride. HgCl.—This well known salt, commonly called *calomel*, is prepared by subliming a mixture of mercurous sulphate and sodium chloride in proper proportions. In order to obtain the product in the form of a soft, fine powder, the vapors are conducted into a spacious chamber into which steam is introduced simultaneously; the presence of aqueous vapor also frees the sublimate from mercuric chloride, some of which is always formed, by solution in the condensed water. Thus obtained, the product is

known as hydrosublimed calomel and is recognized in the German Pharmacopœia as *hydrargyrum chloratum vapore paratum.* When mercurous chloride is sublimed without steam it becomes necessary to reduce the crystalline sublimate to fine powder and wash it thoroughly with water until the washings are no longer affected by ammonia water or ammonium sulphide, showing the complete removal of mercuric chloride.

The mercurous sulphate used in the above process is made by moistening mercuric sulphate with water, adding an equivalent amount of mercury (200.6 parts for 296.67 parts of mercuric sulphate), and triturating the mixture until all globules of mercury disappear. The reaction between mercurous sulphate and sodium chloride when heated together is shown by the following equation: $Hg_2SO_4 + 2NaCl = 2HgCl + Na_2SO_4$.

The Pharmacopœia requires that mild mercurous chloride, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 99.6 per cent. of pure mercurous chloride, which is determined by dissolving a definite quantity, accurately weighed, in an excess of tenth-normal iodine solution with addition of potassium iodide, and triturating the excess of iodine with tenth-normal sodium thiosulphate solution. The reactions involved in this assay consist in the conversion of the mercurous chloride into mercurous iodide by the potassium iodide, $HgCl + KI = HgI + KCl$, and the subsequent conversion of this salt into mercuric iodide by the iodine, $HgI + I = HgI_2$, the mercuric salt being held in solution by the excess of potassium iodide. As each molecule, or 236.06 Gms., of mercurous chloride requires 1 atom, or 126.92 Gms., of iodine, each mil. (or Cc.) of the tenth-normal iodine solution consumed, containing 0.012692 Gm. of iodine, corresponds to 0.023606 Gm. of pure HgCl.

For the electrolytic assay of mild mercurous chloride (0.5–0.6 Gm., accurately weighed, is introduced into a mercury cathode cup (see under Mercury), previously weighed with its mercury, and the process then carried out exactly as directed under Ammoniated Mercury on page 653. Since 1 Gm. of metallic mercury corresponds to 1.1768 Gms. of pure mercurous chloride, the increase of weight of mercury in the cathode cup, when multiplied by 1.1768 and then by 100 and divided by the weight of mild mercurous chloride taken for the assay, will express the per cent. of pure HgCl present in the sample.

In France very finely divided calomel, prepared by precipitation, as directed by the Pharmacopœia of that country, is known as *précipité blanc*, which, translated, means white precipitate; care is necessary not to confound this with ammoniated mercury, known in this country as white precipitate, when dispensing French prescriptions.

The appearance of mild mercurous chloride depends largely upon the degree of mechanical division; while usually white, the finer the powder the more yellowish the tint. When exposed to light it gradually undergoes decomposition and assumes a grayish color, mercuric chloride

being formed, with the elimination of mercury; it must therefore be carefully protected from light.

Calomel has sometimes been prescribed by continental physicians under the names "*aqulia alba*" and "*mercurius dulcis.*"

Yellow Mercurous Iodide, also known as yellow iodide of mercury and protoiodide of mercury. HgI.—The manufacture of mercurous iodide involves two distinct steps. First, mercurous nitrate is made by treating mercury with a mixture of nitric acid and water, in a dark place, until reaction ceases and a little mercury remains undissolved; the salt separates in the form of crystals having the composition $HgNO_3 + H_2O$, which are drained and dried on paper in the dark. The crystallized mercurous nitrate is then dissolved in distilled water acidulated with nitric acid, and to this solution is added, slowly and with constant stirring, a solution of potassium iodide in water, when the following reactions occurs: $(HgNO_3 + H_2O) + KI = HgI + KNO_3 + H_2O$. The precipitate is washed with successive portions of distilled water to remove all potassium nitrate and free acid, and lastly dried on paper in the dark, at a temperature not exceeding 40° C. (104° F.).

The addition of nitric acid is made to prevent the formation of a basic compound, which might otherwise occur; it is also important that the potassium iodide be added to the mercurous nitrate, lest, by a reversal of the process, mercuric salt be formed, which enters into solution as potassium mercuric iodide, while mercury is precipitated, a reaction well known to occur between alkali iodides and mercurous iodide, and illustrated by the equation $2HgI + 2KI = (HgI_2 + 2KI) + Hg$.

Mercurous iodide must be carefully protected from light, as it readily undergoes decomposition. The color of the salt when pure is bright yellow; hence all preparations of a green or greenish-yellow color must be looked upon as impure, the latter colors being due to admixture of metallic mercury, which in a finely divided state is blue, and consequently causes a greenish mixture with the pure yellow salt.

The Pharmacopœia requires that yellow mercurous iodide, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 99 per cent. of pure mercurous iodide, which is determined by adding an accurately weighed quantity of the compound to an excess of tenth-normal iodine solution together with some potassium iodide, and titrating the excess of iodine with tenth-normal sodium thiosulphate solution. The mercurous iodide is oxidized to mercuric iodide, as shown under Mild Mercurous Chloride, which is held in solution by the potassium iodide. Each mil. (or Cc.) of tenth-normal iodine solution consumed in the official assay, corresponds to 0.032752 Gm. of pure HgI.

For the electrolytic assay of yellow mercurous iodide 0.7–0.8 Gm.,

accurately weighed, is introduced into a mercury cathode cup (see under Mercury) previously weighed with its mercury, and the process then carried out exactly as directed under Ammoniated Mercury. Since 1 Gm. of metallic mercury corresponds to 1.6327 Gms. of pure mercurous iodide, the increase of weight of mercury in the cathode cup, when multiplied by 1.6327 and then by 100, and divided by the weight of yellow mercurous iodide taken for the assay, will express the per cent. of pure HgI in the sample.

Green iodide of mercury was at one time largely used, having been recognized in the Pharmacopœias of 1870 and 1880, but its production is due to a faulty process of preparation. When mercury and iodine, or mercury and mercuric iodide, are triturated together, yellow mercurous iodide is formed with variable proportions of mercuric iodide, some of the mercury remaining uncombined in a finely divided form; upon subsequent washing with alcohol the mercuric iodide is removed leaving the insoluble mercurous salt intimately mixed with finely divided mercury, and of a green color. Similar results are likely to occur if mercurous iodide be precipitated from strong neutral solutions of mercurous nitrate by means of potassium iodide; hence the use of a dilute acid solution.

Mercurous iodide has been associated with syrup of ferrous iodide in prescriptions, but such mixtures are incompatible, metallic mercury being deposited, a reaction similar to that explained above taking place, and mercuric iodide held in solution by the ferrous iodide.

Corrosive Mercuric Chloride. $HgCl_2$.—This compound, more familiarly known as corrosive sublimate, and also as bichloride of mercury, mercuric chloride and perchloride of mercury, is obtained by sublimation of an intimate mixture of mercuric sulphate and sodium chloride, both in the form of powder. Mercuric chloride is formed as the result of mutual decomposition; thus, $HgSO_4 + 2NaCl = HgCl_2 + Na_2SO_4$. The heat necessary for the process is likely to decompose some of the mercuric sulphate, with the formation of mercurous chloride, which is volatilized and sublimed along with the mercuric salt.

The Pharmacopœia requires that corrosive mercuric chloride, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 99.5 per cent. of pure $HgCl_2$, which is determined gravimetrically as mercuric sulphide, by passing hydrogen sulphide through a cold weak aqueous solution of the salt and then proceeding exactly as directed for the gravimetric assay of ammoniated mercury on page 653. Since 1 Gm. of mercuric sulphide corresponds to 1.167 Gms. of pure mercuric chloride, or 0.862 + Gm. of metallic mercury, the weight of mercuric sulphide obtained, when multiplied by 1.167 and then by 100, and divided by the weight of corrosive mercuric chloride taken for the assay, will express the per cent. of pure $HgCl_2$ present in the sample. Or as 1 Gm. of pure mercuric chloride is capable of

producing 0.8569 Gm. of mercuric sulphide, the weight of the latter obtained in the official assay, when divided by 0.008569 (0.8569 ÷ 100) and then divided by the weight of the salt taken, will also express the per cent. of pure $HgCl_2$ present.

As each Gm. of metallic mercury corresponds to 1.3535 Gms. of mercuric chloride, the purity percentage of the salt can be determined electrolytically as follows: Dissolve 0.3–0.4 Gm. of the salt, accurately weighed, in 10 mils. (or Cc.) of distilled water and transfer the solution to a mercury cathode cup which has previously been weighed with its mercury (see under Mercury). Dilute the liquid to about 20 mils. (or Cc.) with distilled water, add 1 mil. (or Cc.) of nitric acid diluted with an equal volume of water and 10 mils. (or Cc.) of toluene, and then proceed exactly as directed under Mercury. Having ascertained the increase of weight of the metallic mercury, multiply the same by 1.3535 and then by 100 and divide the product by the weight of the salt originally taken for the assay; the quotient will express the per cent. of pure $HgCl_2$ present in the sample.

Commercial mercuric chloride occurs in heavy crystalline masses, and is usually contaminated somewhat with calomel; hence perfectly clear solutions can rarely be obtained, even with distilled water. For dispensing purposes only the chemically pure article obtained by recrystallization should be used.

Aqueous solutions of mercuric chloride, if exposed to light, gradually undergo decomposition, liberating hydrochloric acid and depositing calomel. The presence of ammonium chloride, however, prevents the change.

Red Mercuric Iodide, also known as *Biniodide of Mercury* and *Red Iodide of Mercury,* and formerly also as *Deutoiodide of Mercury.* HgI_2.—This salt is prepared by mutual decomposition between mercuric chloride and potassium iodide, by pouring a solution of 40 Gms. of the former salt and a solution of 50 Gms. of the latter, simultaneously, into a large volume of water with active stirring, when the following reaction occurs: $HgCl_2 + 2KI = HgI_2 + 2KCl$. An excess of either salt must be avoided, since loss by formation of a soluble compound would result, an excess of potassium iodide producing potassium mercuric iodide ($HgI_2 + 2KI$) and an excess of mercuric chloride causing the formation of mercuric iodochloride ($HgI_2 + 2HgCl_2$ or $Hg_3I_2Cl_4$).

The Pharmacopœia requires that red mercuric iodide, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 99 per cent. of pure HgI_2. As 1 Gm. of metallic mercury corresponds to 2.2654 Gms. of red mercuric iodide, the percentage purity of this salt can be determined electrolytically as follows: Introduce a definite weight (1.0 to 1.2 Gms.) of red mercuric iodide, accurately weighed, into a mercury cathode cup (see under Mercury), which has been previously weighed with its metallic mercury, and then

proceed exactly as directed under Ammoniated Mercury. Having ascertained the increase of weight of the metallic mercury, multiply the same by 2.2654 and then by 100 and divide the product by the weight of the salt taken for the assay; the quotient will express the exact per cent. of pure red mercuric iodide present in the sample.

Mercuric iodide is dimorphous, occurring crystallized both in the form of scarlet-red quadratic octahedra and yellow rhombic prisms, but the Pharmacopœia recognizes the salt only in the form of an amorphous scarlet-red powder, which is obtained by the method of preparation given above. When exposed to light, mercuric iodide gradually becomes paler in color, and should therefore be preserved in dark bottles. It is soluble in solutions of metallic iodides and sodium thiosulphate, as well as alcohol, olive oil, castor oil, chloroform, glycerin, and glacial acetic acid, forming colorless solutions in each case.

Mercuric Salicylate. $Hg.C_6H_4O.CO_2$.—This compound may be obtained by digesting freshly prepared and thoroughly washed yellow oxide of mercury with salicylic acid and a little water on a boiling water-bath until the mass has become snow-white and free from yellow tint. The mercuric salicylate is then collected on a filter and washed with warm water until the filtrate is no longer acid in reaction, dried on porous plates at 30°–40° C. (86°–104° F.) and finally at 100° C. (212° F.). It occurs as a very fine white, or slightly yellowish or slightly pinkish, amorphous, odorless and tasteless powder, which is insoluble in water and alcohol, but soluble in warm solutions of the alkali bromides, chlorides and iodides with the formation of double salts.

The Pharmacopœia requires that mercuric salicylate shall contain not less than 54 per cent., nor more than 59.5 per cent. of mercury which is determined by converting the salt into mercurous chloride and treating this with tenth-normal iodine solution. The digestion of mercuric salicylate with a mixture of sulphuric and nitric acids, as directed in the official assay, causes its decomposition with formation of mercuric sulphate and nitration products of the salicylic acid; the mixture assumes a red color and brown oxides of nitrogen are given off. When the solution is diluted with water it becomes yellow. The hydrogen dioxide solution is added to oxidize anything that would tend to reduce the mercury to the metallic state and thus contaminate the mercurous chloride which is formed subsequently upon addition of the hypophosphorous acid and sodium chloride. The solution remains clear until the sodium chloride is added, which furnishes the hydrochloric acid necessary for the formation of the mercurous chloride. When the washed mercurous chloride is treated with tenth-normal iodine solution and potassium iodide, mercuric iodide is formed as explained on page 654 and kept in solution by the potassiun iodide. As each mil. (or Cc.) of the tenth-normal iodine solution consumed corresponds to 0.02006 Gm. of mercury, the number of mils. (or Cc.)

required in the official test, when multiplied by 2.006 (0.02006 × 100) and divided by the weight of mercuric salicylate taken will express the per cent. of mercury present.

The percentage of mercury present in mercuric salicylate can also be determined electrolytically by introducing 0.7–0.8 Gm. of the compound, accurately weighed, into a mercury cathode cup (see under Mercury), which has been previously weighed with its mercury and then proceeding exactly as directed for the electrolytic assay of Ammoniated Mercury. The increase of weight of the metallic mercury in the cathode cup, when multiplied by 100 and then divided by the weight of mercuric salicylate taken for the assay, will express the per cent. of mercury present in the sample.

Yellow Mercuric Oxide. HgO.—This compound is prepared by pouring a strong solution of mercuric chloride slowly and with constant stirring into a dilute solution of sodium hydroxide; amorphous mercuric oxide is precipitated, while sodium chloride enters into solution. The mixture is allowed to stand at a moderate temperature for an hour to facilitate complete decomposition, after which the liquid is decanted and the precipitate repeatedly washed until free from alkali, drained, and dried on paper, in a dark place, at a temperature of 30° C. (86° F.).

Mercuric salts do not form hydroxides when added to alkali hydroxides, but mercuric oxide is precipitated instead, as shown by the equation $HgCl_2 + 2NaOH = HgO + 2NaCl + H_2O$. It is important that the alkali be used in excess, otherwise a dark-colored oxychloride will be formed; hence the mercuric chloride solution is poured into the alkali solution. It is essential that the sodium hydroxide used be free from carbonate, otherwise mercuric carbonate will be formed. Potassium hydroxide may be used in place of sodium hydroxide, but ammonia is inadmissible, owing to the formation of ammoniated mercury. In order to insure a bright orange-yellow product, heat and light must be excluded during precipitation and drying; unless protected from light, the color of the oxide gradually darkens on keeping, and if exposed to direct sunlight decomposition rapidly occurs.

The Pharmacopœia requires that yellow oxide of mercury, when dried to constant weight at 150° C. (302° F.), shall contain not less than 99.5 per cent. of pure HgO, which is determined by titrating a solution of the oxide in diluted nitric acid with tenth-normal potassium sulphocyanate solution. The reactions involved in this assay result in formation of mercuric nitrate and the conversion of this into mercuric sulphocyanate, thus: $HgO + 2HNO_3 = Hg(NO_3)_2 + H_2O$ and $Hg(NO_3)_2 + 2KCNS = Hg(CNS)_2 + 2KNO_3$, 1 molecule, or 216.6 Gms., of mercuric oxide requiring 2 molecules, or 194.48 Gms., of potassium sulphocyanate for complete conversion; hence each mil. (or Cc.) of tenth-normal potassium sulphocyanate solution, containing 0.009724 Gm. of the salt, corresponds to 0.01083 Gm. of mercuric

oxide. The number of mils. (or Cc.) of tenth-normal potassium sulphocyanate solution consumed before appearance of a permanent yellowish-red color, when multiplied by 1.083 (0.01083 × 100) and then divided by the weight of yellow oxide of mercury taken for the assay will express the per cent. of pure HgO present in the sample.

As 1 Gm. of metallic mercury corresponds to 1.0798 Gms. of yellow mercuric oxide, the purity percentage of the compound can also be determined electrolytically by dissolving a definite quantity of the same in diluted nitric acid and proceeding exactly as explained under Mercury. Having ascertained the increase of weight of the metallic mercury in the cathode cup, multiply the same by 1.0798 and then by 100 and divide the product by the weight of yellow oxide of mercury taken for the assay; the quotient will express the per cent. of pure HgO present in the sample.

Yellow mercuric oxide, being in a state of very fine division, is more active and more sensitive than the red oxide; it is chemically identical with the latter, but differs from it in the molecular arrangement of its particles, being devoid of all crystalline structure. When digested with a solution of oxalic acid, yellow mercuric oxide forms white mercuric oxalate, while the red oxide remains unaffected.

Red Mercuric Oxide. HgO.—Although the name "red precipitate" is commonly applied to this compound, it is never obtained by precipitation, but always by calcination. As a rule mercuric nitrate is triturated with metallic mercury until the latter is extinguished; the mixture is then heated in a porcelain dish until yellowish or reddish vapors cease to be evolved and mercuric oxide remains. The metallic mercury is oxidized at the expense of the nitric acid expelled from the mercuric nitrate, and the process may be illustrated by the following equation: $2Hg(NO_3)_2 + Hg_2 = 4HgO + 4NO_2$.

The Pharmacopœia requires that red mercuric oxide, when dried to constant weight at 150° C. (302° F.), shall contain not less than 99.5 per cent. of pure HgO, which can be determined both volumetrically and electrolytically, exactly in the same manner as directed for the assay of yellow oxide of mercury.

Red mercuric oxide occurs as a crystalline powder or in crystalline scales of an orange-red color, and by trituration with alcohol is gradually converted into a yellowish-red powder. When exposed to light, it darkens in color, but more slowly than the yellow oxide, and, unlike the latter, it is not affected by hot solution of oxalic acid.

Mass of Mercury, also known as *Blue Mass.*—The preparation of this well known mass has been mentioned on page 426. The Pharmacopœia requires that it shall contain not less than 32 per cent., nor more than 34 per cent. of metallic mercury, which is determined by first destroying all organic matter with sulphuric acid, nitric acid and potassium permanganate, the mercury present being converted into

mercuric nitrate; this is then titrated with tenth-normal potassium sulphocyanate solution to the production of a pink tint. Each mil. (or Cc.) of the tenth-normal solution containing 0.009718 Gm. of potassium sulphocyanate required in the official assay corresponds to 0.01003 Gm. of metallic mercury.

Mercurial Ointment.—The composition of this ointment is stated on page 484. The Pharmacopœia requires that the official ointment shall contain not less than 49 per cent., nor more than 51 per cent. of metallic mercury, which is determined by washing an accurately weighed portion of the ointment repeatedly with warm purified petroleum benzin until all fatty matter has been removed; the residue of mercury is then treated with diluted hydrochloric acid, washed with water and finally dried on bibulous paper and dried. Owing to the inflammable nature of the benzin great care is necessary in making this assay, the flame should be removed after melting the ointment and the purified benzin should be warmed by placing the bottle containing it in warm water.

This is the ointment of mercury to be dispensed when prescribed by physicians and it should not be confounded with the article usually called for as Blue Ointment, which latter is official under the name Diluted Mercurial Ointment and contains but 30 per cent. of metallic mercury. When assayed as directed above, diluted mercurial ointment should contain not less than 29 per cent., nor more than 31 per cent. of metallic mercury.

Poison Tablets of Corrosive Mercuric Chloride.—These tablets have been discussed on page 448. The Pharmacopœia requires that each tablet weighing about 1 Gm. shall contain not less than 0.45 Gm., nor more than 0.55 Gm. of corrosive mercuric chloride, which is determined gravimetrically as mercuric sulphide as directed under Corrosive Mercuric Chloride and using one tablet for the assay. The weight of mercuric sulphide obtained, when multiplied by 1.167 indicates its equivalent in pure $HgCl_2$. Tablets of corrosive mercuric chloride may also be assayed electrolytically in the manner directed for the assay of corrosive mercuric chloride.

CHAPTER LI.

THE COMPOUNDS OF ANTIMONY, ARSENIC, AND BISMUTH.

WHILE, at one time, the preparations of antimony formed an important part of the physician's armamentarium, they are but rarely prescribed at the present time; those of arsenic and bismuth, however, are still looked upon as valuable remedial agents. The Pharmacopœia recognizes 1 chemical compound of antimony, 2 compounds of arsenic, besides 4 arsenical solutions, and 5 compounds of bismuth. as shown by the following list:

English name.	Latin name.
Antimony and Potassium Tartrate,	Antimonii et Potassii Tartras.
Arsenous Iodide,	Arseni Iodidum.
Arsenic Trioxide,	Arseni Trioxidum.
Solution of Arsenous Acid,	Liquor Acidi Arsenosi.
Solution of Arsenous and Mercuric Iodides,	Liquor Arseni et Hydrargyri Iodidi.
Solution of Potassium Arsenite,	Liquor Potassii Arsenitis.
Solution of Sodium Arsenate,	Liquor Sodii Arsenatis.
Bismuth and Ammonium Citrate,	Bismuthi et Ammonii Citras.
Bismuth Subcarbonate,	Bismuthi Subcarbonas.
Bismuth Subgallate,	Bismuthi Subgallas.
Bismuth Subnitrate,	Bismuthi Subnitras.
Bismuth Subsalicylate,	Bismuthi Subsalicylas.

THE COMPOUNDS OF ANTIMONY.

Antimony and Potassium Tartrate. $\mathbf{K(SbO)C_4H_4O_6 + \frac{1}{2}H_2O}$.—This salt, which has been known for over two hundred and fifty years, is prepared by boiling a mixture of acid potassium tartrate and antimonous oxide with water for some time, filtering the liquid, concentrating by evaporation, and crystallizing. The British Pharmacopœia directs that a paste be made of the antimonous oxide, cream of tartar, and a small quantity of water, which is set aside for twenty-four hours to allow combination to take place, after which more water is added and the mixture boiled for fifteen minutes, to bring all the newly formed double tartrate into solution.

If pure materials be used, the full theoretical yield is generally obtained; but if the antimonous oxide be contaminated with oxychloride, some of the salt will be lost by refusing to crystallize in the acid liquid. The following equation, $Sb_2O_3 + 2KHC_4H_4O_6 = 2(K(SbO)C_4H_4O_6 + \frac{1}{2}H_2O)$, explains the formation of antimony and potassium tartrate, the univalent group SbO, known as antimonyl,

replacing the hydrogen in the acid potassium tartrate, water being formed at the same time.

The synonyms tartar emetic and tartrated antimony are largely used for this compound, the former being the name generally employed in commerce. The salt is recognized in the British Pharmacopœia as *antimonium tartaratum*, and in the German Pharmacopœia as *tartarus stibiatus*. It is generally sold in powder form, obtained by trituration of the crystals. Aqueous solutions of tartar emetic gradually develop fungi, and on that account cannot be kept on hand for any length of time, nor can they be mixed with strongly alcoholic liquids without precipitation, as the salt is insoluble in alcohol.

The Pharmacopœia requires not less than 98.5 per cent. purity for tartar emetic, the valuation being made with tenth-normal iodine solution in the presence of sodium bicarbonate and starch solution. The iodine, acting as an oxidizing agent, converts the antimonyl into meta-antimonic acid, hydriodic acid and sodio-potassium tartrate being also formed; the object of adding sodium bicarbonate is to neutralize the two newly formed acids, thereby preventing decomposition of the hydriodic acid by the meta-antimonic acid, which would liberate iodine and thus vitiate the end reaction. The official directions to begin titration immediately after addition of the sodium bicarbonate solution are intended to prevent the separation of antimonous oxide, caused by action of the alkali bicarbonate on the antimony and potassium tartrate, a reaction known to occur if the two salts are kept together in solution for some time. The equation $2(K(SbO)C_4H_4O_6 + \frac{1}{2}H_2O) + I_4 + 8NaHCO_3 = 2NaSbO_3 + 4NaI + 2KNaC_4H_4O_6 + 8CO_2 + 5H_2O$ shows that two molecules (or 664.68 parts) of crystallized tartar emetic require 2 molecules (or 507.68 parts) of iodine for complete oxidation of the antimony present; hence each mil. (or Cc.) of tenth-normal iodine solution consumed in the official assay and containing 0.012692 Gm. of iodine must correspond to 0.016617 Gm. of $K(SbO)C_4H_4O_6 + \frac{1}{2}H_2O$, for $507.68 : 664.68 :: 0.012692 : x$ ($x = 0.016617$).

The following compounds of antimony are no longer recognized in the U. S. Pharmacopœia, but are official in the British Pharmacopœia, and therefore deserving of consideration: antimony oxide, and sulphurated antimony.

Antimony Oxide. Antimonous Oxide. Antimony Trioxide. Sb_2O_3.—This compound is obtained by first preparing a solution of antimony trichloride, $SbCl_3$, from antimonous sulphide and hydrochloric acid, pouring this into water, whereby antimony oxychloride, $2SbCl_3 + 5Sb_2O_3$ (known as powder of Algaroth), is precipitated, which is then repeatedly washed with water and mixed with a solution of sodium carbonate, converting the oxychloride into pure oxide, with elimination of carbon dioxide and formation of sodium chloride;

thus, $(2SbCl_3 + 5Sb_2O_3) + 3Na_2CO_3 = 6Sb_2O_3 + 6NaCl + 3CO_2$. In place of sodium carbonate, ammonia water is frequently employed. After proper washing of the oxide it is dried at a temperature not exceeding 100° C. (212° F.), so as to avoid the formation of higher oxides.

Antimony oxide is used in the manufacture of tartar emetic and antimonial powder. The latter preparation is recognized in the *National Formulary* and in the British Pharmacopœia, and is made by mixing 1 part of antimony oxide thoroughly with 2 parts of calcium phosphate; it is also known as James' Powder.

Sulphurated Antimony.—This preparation is defined in the British Pharmacopœia to be a mixture of antimony sulphides and oxides with some sulphur. Commercially it is often designated as *golden sulphuret of antimony* or *golden sulphur*, and is recognized in the German Pharmacopœia as *stibium sulphuratum aurantiacum*, the German name being *Goldschwefel*, which is identical with golden sulphur. Sulphurated antimony, as recognized abroad, is not identical with the sulphurated antimony or Kermes Mineral, at one time official in our Pharmacopœia. The directions for its manufacture are to boil for two hours a mixture of purified antimony sulphide and sulphur with solution of sodium hydroxide, whereby sodium sulphide is formed which, reacting with sulphur and antimonous sulphide, yields sodium sulphantimonate, a compound known as Schlippe's Salt—thus, $Sb_2S_3 + S_2 + 3Na_2S = 2Na_3SbS_4$; some antimonous oxide is also formed by action of the alkali and remains mixed with the other precipitate obtained when diluted sulphuric acid is added to the solution of sodium sulphantimonate, which consists almost wholly of antimony pentasulphide; the resulting hydrogen sulphide escapes, and sodium sulphate remains in solution, as shown by the equation $2Na_3SbS_4 + 3H_2SO_4 = Sb_2S_5 + 3H_2S + 3Na_2SO_4$. The presence of antimony trisulphide is due to possible formation of sodium sulphantimonite during the boiling of the alkaline mixture, and its subsequent decomposition by the acid.

THE COMPOUNDS OF ARSENIC.

Arsenous Iodide. AsI_3.—Arsenic is capable of forming several compounds with iodine, of which, the one indicated by the above formula and more particularly known as arsenic tri-iodide, is alone recognized in the Pharmacopœia. It may be obtained by fusing, in a loosely stoppered test tube or bottle, a mixture of 4 Gms. of metallic arsenic and 20 Gms. of iodine, and pouring the melted mass on a porcelain slab to cool. Some manufacturers prefer to make it by adding finely powdered metallic arsenic to a solution of iodine in carbon disulphide until all color of iodine has disappeared, then concentrating and crystallizing the solution.

The Pharmacopœia requires that arsenous iodide, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 99 per cent. of pure arsenous iodide, which is determined by adding an excess of tenth-normal silver nitrate solution to a solution of arsenous iodide and titrating the excess of silver solution with tenth-normal potassium sulphocyanate solution. As each molecule, or 455.72 Gms. of pure arsenous iodide requires 3 molecules, or 509.67 Gms., of silver nitrate for complete precipitation, each mil. (or Cc.) of the tenth-normal solution, containing 0.016989 Gm. of silver nitrate consumed in the official assay must correspond to 0.015191 Gm. of pure AsI_3, for $509.67 : 455.72 : : 0.016989 : x$ ($x = 0.015191$).

Arsenous iodide must be carefully protected from air and light, otherwise it undergoes decomposition, losing iodine and becoming insoluble in water. Its aqueous solution gradually changes, arsenous and hydriodic acids being formed. The chief use made of the compound is in the preparation of the official solution of arsenous and mercuric iodides, also known as Donovan's Solution.

Arsenic Trioxide. As_2O_3.—This compound has been known for centuries, and although it is still designated as arsenous acid by some Pharmacopœias, the name arsenic trioxide, or arsenous anhydride, seems more in conformity with its true character, since the dry substance evinces no acid properties whatever, and shows only a feeble acid reaction even when dissolved in water. It is obtained chiefly as a by-product in the roasting of tin, cobalt, and nickel ores, and is subsequently purified by sublimation.

Arsenic trioxide occurs in two distinct varieties, an amorphous, vitreous (glass-like) form and a crystalline, opaque, porcelain-like variety, the former being gradually converted into the latter upon exposure to moist air. The solubility of the two varieties in water differs materially, the vitreous being nearly three times as soluble as the porcelain-like variety, but the solubility of both is increased by the presence of hydrochloric acid or alkali hydroxides and carbonates, alkali arsenites being formed in the last two cases. When arsenic trioxide is dissolved in water arsenous acid is formed; thus, $As_2O_3 + 3H_2O = 2H_3AsO_3$, which, however, cannot be isolated, as upon evaporation of the solution arsenic trioxide is again obtained. While alcohol exerts but a slight solvent effect on either variety, glycerin will dissolve about one-fifth of its weight of both, again depositing a portion, however, upon dilution with water, and oil of turpentine dissolves the vitreous but not the opaque variety.

Although the synonym *white arsenic* is frequently applied, it should be borne in mind that the commercial product in powder form, known as white arsenic, is often impure and unfit for pharmaceutical purposes. Arsenic trioxide should never be purchased in powder form, except in bottles bearing on the label the name of some reputable manufacturer or dealer.

The quality of arsenic trioxide can be readily ascertained by titration with tenth-normal iodine solution, which converts arsenous into arsenic acid. The Pharmacopœia requires that official arsenic trioxide, when dried to constant weight at 100° C. (212° F.), shall contain not less than 99.8 per cent. of pure arsenic trioxide, which is determined by dissolving a small quantity, accurately weighed, in boiling water with the aid of sodium hydroxide solution, then exactly neutralizing the solution with diluted sulphuric acid and, when cool, dissolving in the liquid some sodium bicarbonate and titrating with tenth-normal iodine solution. Since 1 molecule, or 197.92 Gms., of pure arsenic trioxide requires 2 molecules, or 507.68 Gms., of iodine for complete oxidation, each mil. (or Cc.) of the tenth-normal solution consumed in the official assay, and containing 0.012692 Gm. of iodine, must correspond to 0.004948 Gm. of pure As_2O_3, for $507.68 : 197.92 :: 0.012692 : x$ ($x = 0.004948$). The addition of sodium bicarbonate is made for the purpose of neutralizing the acids formed, thus preventing the constant liberation of iodine through decomposition of the hydriodic acid by the arsenic acid.

Solution of Arsenous Acid.—This is simply a solution of arsenous acid in water, containing also 5 per cent. of official diluted hydrochloric acid, which latter is added solely to facilitate solution of the arsenous oxide, no chemical action taking place. Formerly this preparation was called solution of chloride of arsenic, under a false impression; arsenous chloride, As_2Cl_6, can be obtained by treating arsenic trioxide with strong hydrochloric acid, but upon being dissolved in water it is again split up into the compounds from which it was made.

The Pharmacopœia requires that the solution shall contain an amount of arsenous acid equivalent to not less than 0.975 per cent. nor more than 1.025 per cent. of pure As_2O_3, which is determined by titration with tenth-normal iodine solution, as in the case of the valuation of arsenic trioxide. One Gm. of solution of arsenous acid, if of official strength, should require not less than 1.97 nor more than 2.07 mils. (or Cc.) of tenth-normal iodine solution for oxidation. The reaction has been fully explained in the preceding article.

Solution of Arsenous and Mercuric Iodides.—Red mercuric iodide, which alone is almost insoluble in water, becomes soluble in the presence of arsenous iodide, and in preparing the above solution the two iodides are triturated together and then mixed with distilled water, when solution readily takes place. It is important that the arsenous iodide be of good quality, otherwise an insoluble residue will remain. The solution contains in every Gm. 0.010 Gm. each of arsenous and mercuric iodide (corresponding to about 4.57 grains of each in every fluidounce), and should be preserved in small, well stoppered vials, in a dark place, as it is prone to decompose. When freshly made

it is of a pale straw-color, and, if this changes to reddish or red, iodine has been liberated, and the solution should not be dispensed.

The Pharmacopœia requires that this solution shall contain not less than 0.95 per cent. nor more than 1.05 per cent. each of pure arsenous iodide and mercuric iodide. The percentage of arsenous iodide present is determined by adding sodium bicarbonate to a diluted portion of the solution and then titrating with tenth-normal iodine solution to the appearance of a permanent blue color, starch test-solution being used as indicator, each mil. (or Cc.) of the tenth-normal solution consumed corresponding to 0.022786 Gm. of pure AsI_3. The mercuric iodide content is assayed by first reducing an accurately weighed portion of the solution with formaldehyde in the presence of potassium hydroxide, then washing the metallic mercury obtained carefully, dissolving it in diluted nitric acid and titrating the solution with tenth-normal potassium sulphocyanate solution to a permanent pink color, using ferric ammonium sulphate test-solution as indicator; each mil. (or Cc.) of the tenth-normal potassium sulphocyanate solution required corresponds to 0.022722 of pure HgI_2.

This preparation is better known as Donovan's Solution, and was at one time considered a valuable remedial agent, but is little used at present.

Solution of Potassium Arsenite.—This preparation, popularly known as Fowler's Solution, is probably the most extensively employed of all arsenical compounds. It is made by heating arsenic trioxide and potassium bicarbonate with a small quantity of water until perfect solution has been effected, which when cold is diluted with water, and compound tincture of lavender added. The use of a small quantity of water is favorable to chemical union between the alkali and feeble acid. The exact nature of the compound in solution is somewhat in doubt, some authorities believing that when arsenic trioxide and acid potassium carbonate are brought together with water, as in the official process, secondary potassium ortho-arsenite, K_2HAsO_3, is formed according to the equation $As_2O_3 + 4KHCO_3 = 2K_2HAsO_3 + 4CO_2 + H_2O$, while others claim that primary potassium ortho-arsenite, KH_2AsO_3, is produced. Still others assert that potassium meta-arsenite, $KAsO_2$, only is formed according to the equation $As_2O_3 + 2KHCO_3 = 2KAsO_3 + 2CO_2 + H_2O$.

The solution is most conveniently prepared in a small, long-neck flask, or preferably in a beaker covered with a watch-glass, whereby the evaporation of water is materially lessened; the dilution should not be made until the liquid is cold. Solution of potassium arsenite is likely to develop fungi in the course of time, and if an excess of alkali be present, as in the British and German preparations, the arsenous acid is gradually converted into arsenic acid; it is better, therefore, not to keep the solution on hand in large quantities. While the preparations of the United States and British Pharmacopœias are colored reddish by the

compound tincture of lavender added, those of the German and French Pharmacopœias are colorless. The term *liquor arsenicalis* is officially used in Great Britain to designate this solution.

The Pharmacopœia requires that Fowler's Solution shall contain an amount of potassium arsenite corresponding to not less than 0.975 per cent. nor more than 1.025 per cent. of pure arsenic trioxide, which is determined, after acidulation with hydrochloric acid and addition of sodium bicarbonate, by titration with tenth-normal iodine solution, each mil. (or Cc.) of the latter consumed corresponding to 0.004948 Gm. of pure As_2O_3.

Owing to its very poisonous nature, Fowler's Solution should never be dispensed without a physician's prescription, and, although sometimes called for by the public, pharmacists should refuse to sell it, for their own protection as well as that of others.

Solution of Sodium Arsenate.—An aqueous solution of sodium arsenate, containing 0.010 Gm. of the anhydrous salt in each Gm. The object of using anhydrous sodium arsenate is to insure uniformity of strength in the finished product, as the commercial salt may contain variable proportions of water of crystallization (see page 582); the temperature used for desiccation should not be carried beyond 149° C. (300° F.), in order to avoid changing the sodium ortho-arsenate into pyro-arsenate.

The Pharmacopœia requires that the official solution of sodium arsenate shall contain not less than 0.975 per cent., nor more than 1.025 per cent. of anhydrous sodium arsenate, which is determined by heating an accurately weighed portion of the solution with hydrochloric acid and potassium iodide to 80° C. (176° F.) for 15 minutes, and then titrating the liberated iodine with tenth-normal sodium thiosulphate solution. The reactions involved have been explained under Sodium Arsenate on page 583, and show that 253.84 Gms. of iodine will be liberated for every 185.97 Gms. of anhydrous sodium arsenate; hence each mil. (or Cc.) of tenth-normal sodium thiosulphate solution required in the official assay and corresponding to 0.012692 Gm. of iodine must also correspond to 0.0092985 Gm. of Na_2HAsO_4.

This preparation is not identical with Pearson's Arsenical Solution, recognized in the French Pharmacopœia, and prepared by dissolving 1 part of crystallized sodium arsenate in 600 parts of water. As Pearson's Solution is sometimes prescribed in this country, it should be borne in mind that the solution of sodium arsenate of the United States Pharmacopœia is about ten times as strong as the French preparation bearing Dr. Pearson's name. The *National Formulary* states that Pearson's Solution may be made by mixing 1 volume of the official solution of sodium arsenate with 9 volumes of distilled water.

THE COMPOUNDS OF BISMUTH.

Bismuth and Ammonium Citrate.—This scale salt is usually made by adding ammonia water gradually to a smooth paste made of normal bismuth citrate, $BiC_6H_5O_7$, and twice its weight of water, until perfect solution has been effected, which after filtration is concentrated on a waterbath to a syrupy consistence and spread on plates of glass to dry, as directed under Ferric Phosphate. A slight excess of ammonia water will be advantageous in order to maintain a neutral or faintly alkaline reaction during evaporation of the solution, as some ammonia will be lost and an acid condition would cause precipitation.

The exact composition of this compound cannot be definitely stated. By some the view is held that by the action of ammonia bismuthous hydroxide is formed, which is held in solution by the ammonium citrate simultaneously produced, giving the salt the composition indicated by the formula $Bi(OH)_3 + (NH_4)_3C_6H_5O_7 + H_2O$. The Pharmacopœia gives no chemical formula for the compound, but states that it consists of bismuth citrate rendered soluble by the presence of ammonium citrate, and since bismuth citrate, as usually made, contains a slight excess of citric acid some ammonium citrate is undoubtedly formed in the process as stated above.

The Pharmacopœia requires that bismuth and ammonium citrate when dried to constant weight in a desiccator over sulphuric acid, shall yield not less than 46 per cent. nor more than 52 per cent. of bismuth oxide, which is determined by ignition of an accurately weighed portion of the scale salt, previously dried to constant weight, in a porcelain crucible, and after cooling, treating the residue with nitric acid and again igniting to red heat; the final residue consisting of bismuth oxide is then weighed and, if multiplied by 100 and divided by the weight of the salt taken for the assay, will express the per cent. of Bi_2O_3 yielded by the sample.

Bismuth and ammonium citrate in scale form slowly loses ammonia unless preserved in tightly stoppered bottles, thereby becoming opaque and partly insoluble in water. When such a condition exists the cautious addition of a few drops of ammonia water to the turbid mixture usually effects a perfect solution, as in similar cases of the iron scale salts.

Bismuth Betanaphthol.—Owing to the variable composition of this compound, no chemical formula is assigned to it by the Pharmacopœia. It is said to be prepared by action of an alkaline solution of betanaphthol, $C_{10}H_7OH$, on a solution of bismuth trinitrate in glycerin, and occurs as a buff-colored to grayish-brown amorphous powder, nearly insoluble in water, alcohol, chloroform and ether.

The Pharmacopœia requires that bismuth betanaphthol shall yield, upon assay, not less than 15 per cent. of betanaphthol and when thoroughly ignited not less than 73 per cent. nor more than 78 per cent

of bismuth oxide; the latter is determined by incineration of an accurately weighed portion of the salt, dissolving the residue in nitric acid, evaporating the solution to dryness and igniting the residue to constant weight. The per cent. of betanaphthol present is determined by dissolving an accurately weighed portion of the salt in hydrochloric acid and when cool extracting the liberated betanaphthol with successive portions of chloroform, which are then united and allowed to evaporate spontaneously, the residue being dried in a desiccator.

Bismuth Magma, also known as *Milk of Bismuth.*—The preparation of this mixture, sometimes designated as Cream of Bismuth, has been discussed on page 391. The Pharmacopœia requires that it shall yield upon evaporation to dryness and subsequent ignition to constant weight, not less than 5.6 per cent. nor more than 6.2 per cent. of bismuth oxide, Bi_2O_3.

Bismuth Subcarbonate. Bismuthyl Carbonate.—The first step necessary in the manufacture of this compound is the preparation of a solution of pure normal bismuth nitrate, which is then decomposed by means of a cold solution of sodium carbonate. When metallic bismuth is treated with nitric acid, a solution of bismuth trinitrate, $Bi(NO_3)_3$, is formed, and the arsenic which is almost invariably present in bismuth is converted into arsenic acid, and combining with bismuth forms bismuth arsenate, $BiAsO_4$. In order to rid the solution of the latter salt it is diluted with water to incipient turbidity and set aside for twenty-four or thirty-six hours, when nearly all the bismuth arsenate will have been deposited, being less soluble than the nitrate; by adding an excess of ammonia water to the clear solution, all bismuth will be precipitated as bismuthous hydroxide, ammonium nitrate and arsenate remaining in solution. After washing the precipitate until the washings are tasteless, it is redissolved in nitric acid, and the resulting solution of purified bismuth trinitrate slowly added, with constant stirring, to a solution of alkali carbonate. The final precipitate, consisting of basic bismuth carbonate, is thoroughly washed with water and dried with moderate heat.

The exact composition of bismuth subcarbonate depends upon the degree of dilution of the sodium carbonate solution and the temperature at which the bismuth nitrate is added and the final precipitate dried. The Pharmacopœia requires that bismuth subcarbonate when dried to constant weight at 100° C. (212° F.) shall yield not less than 90 per cent. of pure bismuth oxide, when ignited at a red heat. In England the salt is known as bismuth carbonate or bismuth oxycarbonate, the British Pharmacopœia directing the use of ammonium carbonate in place of sodium carbonate.

Bismuth Subgallate. Bismuthyl Gallate.—This compound commercially also known as *dermatol,* may be obtained by dissolving

bismuth trinitrate in glacial acetic acid, diluting the solution with water, and adding, with constant stirring, a warm, weak aqueous solution of gallic acid. The resulting precipitate is separated by decantation and washed until entirely free from nitric acid, and then dried at about 100° C. (212° F.). Its composition may be indicated by the formula $BiOC_7H_5O_5 + H_2O$ or $C_6H_2(OH)_3COOBiO + H_2O$, but it varies somewhat in commercial samples. Bismuth subgallate occurs as a bright yellow powder, insoluble in water, but soluble in solutions of the alkali hydroxides.

The Pharmacopœia requires that bismuth subgallate, when dried to constant weight at 100° C. (212° F.), shall yield not less than 52 per cent. nor more than 57 per cent. of pure bismuth oxide, which is determined by igniting an accurately weighed portion of the compound, treating the residue with nitric acid and again igniting as directed in the assay for Bismuth and Ammonium Citrate.

Bismuth Subnitrate. Bismuthyl Nitrate.—A part of the process of manufacture of this salt has been detailed under Bismuth Subcarbonate. When a solution of purified bismuth trinitrate is poured into water precipitation of a basic salt at once takes place, the nitric acid liberated, however, retaining some of the normal nitrate in solution. As in the case of the carbonate, the composition of the precipitate will vary with the volume and temperature of the water used, and also the temperature at which the salt is dried.

The Pharmacopœia gives no formula for bismuth subnitrate, but requires that when dried for 24 hours in a desiccator over sulphuric acid it shall yield not less than 79 per cent. of pure bismuth oxide, which is determined by igniting an accurately weighed portion of the salt thoroughly at a red heat. The weight of the cold residue, when multiplied by 100 and divided by the weight of bismuth subnitrate taken for the assay, will express the per cent. of Bi_2O_3 obtained.

Although a basic salt, bismuth subnitrate, when mixed with water, shows an acid reaction, due to decomposition and liberation of nitric acid, and should not be dispensed in mixtures containing alkali carbonate or bicarbonates, as decomposition (often with explosive violence) will result (see also page 379).

In continental Europe the salt is frequently prescribed under the name *magisterium bismuthi.*

Bismuth Subsalicylate. Bismuthyl Salicylate.—This basic compound, of variable composition, may be obtained by digesting freshly precipitated bismuth hydroxide with salicylic acid at ordinary temperature for 48 hours, then washing with small quantities of cold water until all free acid has been removed, and finally drying at a low temperature in a dark place.

The Pharmacopœia requires that bismuth subsalicylate, when dried to constant weight at 100° C. (212° F.), shall yield not less than

62 per cent. nor more than 66 per cent. of pure bismuth oxide, which is determined by igniting an accurately weighed portion of the compound, treating the residue with nitric acid and again igniting as directed under Bismuth and Ammonium Citrate.

Among the non-official compounds of bismuth the following are of interest:

Glycerite of Bismuth.—This preparation, recognized in the *National Formulary*, has been discussed on page 279. It consists of a solution of bismuth and sodium tartrate in water and glycerin and is of such strength that 100 mils. (or Cc.) will yield 12.8 Gms. of bismuth oxide, which may be determined by precipitating the bismuth as sulphide, dissolving this in nitric acid, precipitating with ammonia water and ammonium carbonate and finally igniting in the usual manner.

Bismuth Subiodide. Bismuthyl Iodide. BiOI.—This salt is obtained either by boiling an aqueous suspension of bismuth subnitrate with potassium iodide or by heating, but not boiling, a solution of normal bismuth nitrate with potassium iodide. In either case the bright red or brownish-red precipitate is well washed with water and dried at the temperature of boiling water.

CHAPTER LII.

THE COMPOUNDS OF COPPER, LEAD, ZINC, GOLD, SILVER AND URANIUM.

WHILE copper, gold and uranium each furnish but one compound recognized in the Pharmacopœia, the official salts of lead, silver, and zinc are more numerous and of greater importance, as may be seen by the following list:

Official English name.	Official Latin name.
Copper Sulphate,	Cupri Sulphas.
Lead Acetate,	Plumbi Acetas.
Lead Oxide,	Plumbi Oxidum.
Lead Plaster,	Emplastrum Plumbi.
Solution of Lead Subacetate,	Liquor Plumbi Subacetatis.
Metallic Zinc,	Zincum.
Zinc Acetate,	Zinci Acetas.
Precipitated Zinc Carbonate,	Zinci Carbonas Præcipitatus.
Zinc Chloride,	Zinci Chloridum.
Zinc Oxide,	Zinci Oxidum.
Zinc Phenolsulphonate,	Zinci Phenolsulphonas.
Zinc Sulphate,	Zinci Sulphas.
Zinc Valerate,	Zinci Valeras.
Solution of Zinc Chloride,	Liquor Zinci Chloridi.
Ointment of Zinc Oxide,	Unguentum Zinci Oxidi.
Gold and Sodium Chloride,	Auri et Sodii Chloridum.
Silver Nitrate,	Argenti Nitras.
Moulded Silver Nitrate,	Argenti Nitras Fusus.
Silver Oxide,	Argenti Oxidum.
Uranium Nitrate,	Uranii Nitras.

THE COMPOUNDS OF COPPER.

Copper Sulphate. $CuSO_4 + 5H_2O$.—The crude salt, known in commerce as blue vitrol, is not suited for pharmaceutical purposes on account of the impurities (iron and other metals) present; and as these cannot be removed by simple recrystallization, a better article may be obtained by direct solution of metallic copper in diluted sulphuric acid aided by a little nitric acid, the following reaction taking place: $Cu_3 + 3H_2SO_4 + 2HNO_3 = 3CuSO_4 + 2NO + 4H_2O$. The solution may be concentrated and allowed to crystallize or evaporated with frequent stirring, so that the salt will be obtained in the form of a coarse granular powder, which latter is more convenient for dispensing purposes.

The official crystallized cupric sulphate, containing 36.15 per cent. of water, slowly effloresces upon exposure to air; hence it must be

kept in tightly closed vessels. When deprived of all of its water of crystallization at a temperature of 200° C. (392° F.), the white, anhydrous powder remaining forms a valuable dehydrating agent and is used in the preservation of absolute alcohol.

The Pharmacopœia requires that official copper sulphate shall contain not less than 62.97 per cent. nor more than 66.79 per cent. of anhydrous cupric sulphate, corresponding to not less than 98.5 per cent. of the crystallized salt, which is determined by dissolving an accurately weighed portion of the uneffloresced salt in water, adding some acetic acid and potassium iodide, and titrating the liberated iodine with tenth-normal sodium thiosulphate solution. The assay depends upon the decomposition of copper sulphate by potassium iodide when cuprous iodide is formed and iodine liberated, since cupric iodide cannot be obtained, being at once decomposed into cuprous iodide and iodine. The equation $CuSO_4 + 2KI = CuI + I + K_2SO_4$ shows that 1 molecule, or 159.64 Gms., of anhydrous cupric sulphate will yield 1 atom, or 126.92 Gms. of iodine, and hence each mil. (or Cc.) of tenth-normal sodium thiosulphate solution required in the official assay and indicating 0.012692 Gm. of iodine must correspond to 0.015964 Gm. of pure $CuSO_4$.

Among the non-official compounds of copper the following may be mentioned as of interest to pharmacists:

Copper Acetate. $Cu(C_2H_3O_2)_2 + H_2O$ **or** $(CH_3COO)_2Cu + H_2O$.—Crystallized cupric acetate, which was recognized in the Pharmacopœia of 1880, may be obtained by double decomposition of cupric sulphate and lead or calcium acetate; the solution after filtration is acidulated with acetic acid, concentrated, and allowed to crystallize. This salt must not be confounded with ordinary verdigris, a basic cupric acetate, which occurs in amorphous masses and has the composition $Cu_2O(C_2H_3O_2)_2$.

Cuprum Aluminatum.—This compound is recognized in the German and Swiss Pharmacopœias as Cuprum Aluminatum and in the French Pharmacopœia as Pierre Divine, and prescriptions for it under these titles occasionally reach this country; its German name is *Kupferalaun* or *Copper Alum*. It is prepared by fusing together 16 parts each of potassium alum, copper sulphate and potassium nitrate, and, after removal from the fire, adding to the fused mixture, 1 part each of camphor and powdered potassium alum; after thorough incorporation of the powders, the mass is poured on a slab and allowed to solidify.

Aluminated copper occurs in greenish-blue broken pieces and is soluble in 16 parts of water with exception of a small amount of camphor; solutions of it should always be filtered before dispensing them. It is sometimes prescribed under the name Lapis Divinus, given as a synonym in the three Pharmacopœias mentioned above.

THE COMPOUNDS OF LEAD.

Lead Acetate. $Pb(C_2H_3O_2)_2 + 3H_2O$ or $(CH_3COO)_2Pb + 3H_2O$.—This salt may be obtained by dissolving lead in diluted acetic acid or by exposing lead in the form of sheets to the combined action of air and vinegar. The resulting solutions are filtered, concentrated, and crystallized; in order to secure perfect crystallization a little acetic acid is added to the liquid. Large quantities of lead acetate are now made from metallic lead by placing the same in granular form in large open stoneware cylinders and allowing strong acetic acid to fall upon it in drops from a cask provided with a glass outlet tube and a multiple drip cock attachment. During the operation, which is allowed to go on continuously day and night until completed, heat is developed as the acid slowly trickles down over the metal, and under the influence of air the lead is gradually dissolved in the form of basic lead acetate. The solution is allowed to collect in the lower part of the cylinder, and is thence transferred to large receptacles, where it is exactly neutralized with acetic acid, and the solution of normal lead acetate then set aside to crystallize. Purified lead acetate for dispensing purposes is prepared in granular form by dissolving the large crystals in water, filtering and evaporating the solution with frequent stirring, so that small crystals may be produced.

Commercially, lead acetate is better known as *sugar of lead*, on account of its peculiar sweet taste. When exposed to the air it effloresces and slowly absorbs carbon dioxide; it must therefore be preserved in well closed bottles or cans.

The Pharmacopœia requires that official sugar of lead shall contain not less than 85.31 per cent. nor more than 89.57 per cent. of pure anhydrous lead acetate, corresponding to not less than 99.5 per cent. of the crystallized salt, which is determined by adding to a solution of the salt an excess of tenth-normal oxalic acid solution and then after filtration and acidulation of the filtrate with sulphuric acid, titrating the excess of oxalic acid with tenth-normal potassium permanganate solution. The equation $Pb(C_2H_3O_2)_2 + H_2C_4O_4.2H_2O = PbC_4O_4 + 2HC_2H_3O_2 + 2H_2O$ shows that 1 molecule, or 325.152 Gms., of anhydrous lead acetate requires 1 molecule, or 126.05 Gms., of crystallized oxalic acid for complete precipitation, and hence each mil. (or Cc.) of the tenth-normal acid solution consumed in the official assay, and containing 0.0063025 Gm. of crystallized oxalic acid must correspond to 0.016257 Gms. of pure $Pb(C_2H_3O_2)_2$. The solution of lead acetate must be made with recently boiled distilled water to prevent the action of any dissolved air, and it must not be overlooked in the official assay that only one-twentieth of the amount of lead acetate originally taken is represented in the final determination of the excess of oxalic acid with potassium permanganate solution.

Lead Oxide. PbO.—Of the different oxides of lead occurring on the market, only that more particularly known as litharge is officially recognized. It is obtained by heating lead in contact with air to a temperature of about 400° to 450° C. (752° to 842° F.), and also as a by-product in the treatment of silver ores by the process known as cupellation.

When lead oxide is exposed to the air it slowly absorbs moisture and carbon dioxide, a basic lead carbonate being formed; hence it should be kept in well closed vessels; the Pharmacopœia limits the increase in weight due to such absorption to 4 per cent. The color of commercial litharge is not uniform, which is due to the manner of cooling the molten mass; if allowed to cool slowly, a reddish-yellow product is obtained; while if cooled rapidly, a yellowish-red color results.

The Pharmacopœia requires that when freshly ignited, litharge shall contain not less than 96 per cent. of pure lead oxide, which is determined by dissolving an accurately weighed amount of the litharge in a mixture of acetic acid and recently boiled distilled water and then adding to this solution of lead acetate an excess of tenth-normal oxalic acid solution, the excess of oxalic acid being finally titrated with the tenth-normal potassium permanganate solution; each mil. (or Cc.) of the tenth-normal oxalic acid solution consumed corresponds to 0.011155 Gm. of pure lead oxide.

Solution of Lead Subacetate.—An aqueous liquid containing in solution lead subacetate (approximately $Pb_2O(CH_3COO)_2$), corresponding to not less than 18 per cent. of metallic lead. The official directions for preparing this well known solution are to boil for half an hour a mixture of 180 Gms. of lead acetate, 110 Gms. of lead oxide, and 800 mils. (or Cc.) of distilled water, with occasional stirring. When cool, the mixture is filtered and sufficient distilled water, previously boiled and cooled, added to the filtrate to bring the weight of the latter up to 1000 Gms.

The lead acetate should be dissolved in 700 mils. (or Cc.) of boiling distilled water and then added to the lead oxide previously rubbed to a smooth paste with 100 mils. (or Cc.) of distilled water, in divided portions, and slowly with constant stirring. After a thorough mixture has been effected it is then boiled for half an hour to complete the chemical reaction. Distilled water, preferably that which has been boiled, so as to avoid the presence of carbon dioxide, as well as sulphates and chlorides, should always be used in the preparation of this solution. The process of boiling the mixture is directed mainly for the purpose of economizing time, as the same changes will take place even at ordinary temperature, several days, however, being required, together with frequent agitation of the vessel.

The quality of solution of lead subacetate depends largely upon the quality of the lead acetate and lead oxide employed. The following

process, suggested by Haussmann, is admirably adapted for the retail pharmacist's needs, and yields a more satisfactory product than the official method: pour 730 mils. (or Cc.) of distilled water, heated to boiling, into a strong bottle previously warmed and graduated at 730 mils. (or Cc.); add quickly 170 Gms. of pure crystallized lead acetate in small pieces, cork the bottle, and dissolve by gentle agitation. After solution of the salt, add in divided portions 100 Gms. of lead oxide (97–99 per cent. pure), previously sifted, shaking the bottle after each addition. In about ten minutes the yellow color of the lead oxide will disappear, and after two hours all reaction will have ceased. The mixture may then be filtered under cover.

Several basic lead acetates are known, the composition of which depends upon the proportions in which the lead acetate and oxide are employed; thus the United States and British Pharmacopœias, using the acetate and oxide in the proportion of their molecular weights, obtain in solution the basic compound indicated by the formula $Pb_2O(C_2H_3O_2)_2$, according to the equation $(Pb(C_2H_3O_2)_2 + 3H_2O) + PbO = Pb_2O(C_2H_3O_2)_2 + 3H_2O$; while the German and French Pharmacopœias, directing the use of three parts of lead acetate to one of lead oxide, cause the production of a less basic compound, as shown by the equation $2(Pb(C_2H_3O_2)_2 + 3H_2O) + PbO = Pb_3O(C_2H_3O_2)_4 + 6H_2O$.

In the preparation of this solution other basic lead acetates, such as $Pb_3O_2(C_2H_3O_2)_2$, are also formed in small quantities in addition to those mentioned, and an insoluble white residue is always left, consisting of a very basic compound, probably having a composition $Pb_6O_5(C_2H_3O_2)_2$.

Solution of lead subacetate, commercially known as Goulard's Extract, is very sensitive to carbon dioxide, the least exposure to air causing a film of basic lead carbonate to form; hence it must be preserved in tightly stoppered bottles, and should always be filtered in a closely covered funnel. It is incompatible with solution of acacia, differing in this respect from the normal acetate.

The valuation of solution of lead subacetate is made by precipitating all lead present by addition of an excess of tenth-normal oxalic acid solution, and then determining the excess of oxalic acid by means of potassium permanganate solution. From the data thus obtained the percentage of lead subacetate in the solution may be calculated. In the official test an excess of tenth-normal oxalic acid solution is added to an accurately weighed small portion of solution of lead subacetate diluted with recently boiled distilled water; after shaking the mixture for five minutes it is diluted to a definite volume and filtered. One-half of the filtrate after acidulation with sulphuric acid and warming to 70° C. (158° F.), is titrated with tenth normal potassium permanganate solution to determine the excess of oxalic acid. Each mil. (or Cc.) of the tenth-normal oxalic acid solution consumed corresponds to 0.010355 Gm. of metallic lead. The reaction occurring

in the assay may be shown by the following equation: $Pb_2O(C_2H_3O_2)_2 + 2(H_2C_2O_4 + 2H_2O) = 2Pb(C_2O_4) + 2HC_2H_3O + 5H_2O$, from which it is seen that every molecule, or 548.25 Gms., of lead subacetate, representing 1 molecule, or 414.2 Gms., of metallic lead, requires 2 molecules, or 252.1 Gms., of crystallized oxalic acid, and hence 1 mil. (or Cc.) of the tenth-normal solution consumed in the official assay and containing 0.0063025 Gm. of the crystallized acid, must correspond to 0.01035 Gm. of metallic lead. When calculating the per cent. of lead present in the sample, it must not be overlooked that in the official assay only one-half of the filtrate is titrated with tenth-normal potassium permanganate solution.

The Pharmacopœia also recognizes a dilute solution of lead subacetate, made by mixing 40 Gms. of the above solution with 960 Gms. of distilled water, previously boiled and cooled. This preparation is popularly known as lead water.

THE COMPOUNDS OF ZINC.

Zinc.—Metallic zinc is recognized in the Pharmacopœia because it is used in the preparation of the official solution of zinc chloride and as a reagent in some analytical processes. It occurs in nature as zinc blende, impure zinc sulphide, and as impure zinc carbonate in different minerals, and is obtained from these by various methods, such as conversion of the metal into zinc oxide, heating in reverberatory furnaces, etc., which are usually explained in text-books on chemistry.

The Pharmacopœia describes zinc as a bluish-white metal occurring in the form of thin sheets or in granular pieces, or in thin moulded pencils, or in powder form, and having a specific gravity ranging from 6.9 when it is cast to 7.2 when it is rolled. Officially metallic zinc is required to be free from arsenic, phosphorus, sulphur and antimony, and should contain not less than 99 per cent. of pure zinc, which may be determined by dissolving an accurately weighed amount of the metal in hydrochloric acid, then precipitating the zinc as sulphide, after rendering the solution alkaline by addition of ammonia water, and subsequently converting the zinc sulphide into zinc oxide as directed in the assay for Zinc Acetate on page 679. As each molecule, or 130.74 Gms., of pure metallic zinc is capable of producing 2 molecules, or 162.74 Gms., of zinc oxide, 1 Gm. of the latter corresponds to 0.80336 Gm. of the metal; hence the weight of zinc oxide obtained in the official assay, when multiplied by 80.336 (0.80336 × 100) and divided by the weight of zinc taken, will express the per cent. of pure metallic zinc present in the sample.

The Pharmacopœia also permits the assay of metallic zinc and its salts by electrolysis, which must be carried out in nickel dishes of about 175 mils. (or Cc.) capacity. For metallic zinc about 1.5 Gms. of the metal is dissolved in warm diluted sulphuric acid, which solution, after filtration, is made up to 100 mils. (or Cc.); of this solution, 10

mils. (or Cc.) are measured into the nickel dish, previously tared, 30 to 35 mils. (or Cc.) of a 20 per cent. sodium hydroxide solution are added and the liquid diluted to 120 mils. (or Cc.). The mixture is heated nearly to boiling and a current of 4 to 5 amperes and 5 to 6 volts passed through for 30 minutes, stirring the solution by rotating the anode 500 to 600 revolutions per minute. Without interrupting the current, the deposited zinc is washed with distilled water with the aid of a siphon until the current drops to zero or nearly so. The dish is then removed, the zinc is washed first with alcohol and then with ether, and dried in a desiccator over sulphuric acid and weighed. The increase in weight of the dish represents the amount of zinc present in the sample.

For the electrolytic assay of salts of zinc introduce into the tared nickel dish an accurately weighed quantity of the salt, equivalent to about 0.15 Gm. of metallic zinc (zinc acetate, 0.5 Gm.; zinc carbonate, 0.25 Gm.; zinc chloride, 0.3 Gm.; zinc oxide, 0.2 Gm.; zinc phenolsulphonate, 1.2 Gms.; zinc sulphate, 0.6 Gm.; zinc valerate, 0.7 Gm.); dissolve in distilled water or in 10 mils. (or Cc.) of diluted sulphuric acid (zinc carbonate and zinc oxide), add from 30 to 35 mils. (or Cc.) of a 20 per cent. sodium hydroxide solution and dilute with distilled water to about 120 mils. (or Cc.). Then proceed further as directed above for metallic zinc.

Zinc Acetate. $Zn(C_2H_3O_2)_2 + 2H_2O$ **or** $(CH_3COO)_2Zn + 2H_2O$.— This salt may be prepared by solution of either zinc oxide or carbonate in hot, moderately diluted acetic acid. After filtration the solution is allowed to cool, when a large portion of the newly formed salt separates. A further yield of crystals may be obtained by concentration of the mother-liquor. It is better to crystallize the salt from a slightly acid solution, so as to avoid the formation of basic zinc acetate.

Zinc acetate upon exposure to air slowly effloresces and loses acetic acid, a basic salt being formed at the same time; hence it should be preserved in well stoppered bottles.

The Pharmacopœia requires that the salt shall contain not less than 83.16 per cent. nor more than 87.32 per cent. of anhydrous zinc acetate, corresponding to not less than 99.5 per cent. of the crystallized salt, which is determined by precipitating an accurately weighed quantity of the salt as zinc sulphide, dissolving this in hot diluted nitric acid, evaporating to dryness and igniting the residue of zinc oxide. As 1 molecule, or 219.45 Gms., of zinc acetate will yield 1 molecule, or 81.37 Gms. of zinc oxide, each Gm. of the latter corresponds to 2.2541 Gms. of anhydrous or 2.697 Gms. of crystallized zinc acetate, the weight of zinc oxide obtained in the official assay, when multiplied by 225.41 (2.2541×100) and divided by the weight of the salt taken, will express the per cent. of pure anhydrous zinc acetate present in the sample. Each Gm. of official zinc acetate should yield not less than 0.360 Gm. nor more than 0.387 Gm. of zinc oxide.

Zinc acetate may also be assayed electrolytically by determining the amount of zinc present, in the manner described under Zinc on page 679. Each Gm. of metallic zinc thus determined corresponds to 3.357 Gms. of $Zn(C_2H_3O_2)_2 + 2H_2O$.

Precipitated Zinc Carbonate.—This compound is obtained by mutual decomposition between zinc sulphate and sodium carbonate. On mixing cold solutions of these two salts normal zinc carbonate is precipitated in a gelatinous form, but rapidly undergoes decomposition, carbon dioxide being liberated, whereby a portion of the precipitate is again dissolved. If, however, the solution of zinc sulphate be added slowly and with constant stirring to a boiling solution of sodium carbonate, carbon dioxide is rapidly expelled and a basic zinc carbonate precipitated; thus, $5(ZnSO_4 + 7H_2O) + 5(Na_2CO_3 + 10H_2O) = (2ZnCO_3 + 3Zn(OH)_2) + 5Na_2SO_4 + 3CO_2 + 82H_2O$; the mixture is boiled for a short time, after which the precipitate is washed until all sodium sulphate is removed, and then dried at a gentle heat. Potassium carbonate is not so well adapted as the sodium salt for the process, as the resulting potassium sulphate is less readily washed out, and ammonium carbonate is unsuitable, since it does not completely precipitate the zinc.

The composition of commercial zinc carbonate will naturally vary with the particular process employed in its manufacture and the relative proportions of the two salts used, and hence no definite formula can be given for the compound.

Zinc carbonate contains basic carbonate corresponding to not less than 68 per cent. of zinc oxide, which is determined by dissolving an accurately weighed quantity of the salt in an excess of normal sulphuric acid and determining the excess of acid by titration with normal potassium hydroxide solution. As 1 mil. (or Cc.) of normal acid corresponds to 0.040685 Gm. of zinc oxide, the number of mils. (or Cc.) consumed by the basic carbonate in the official assay, when multiplied by 4.0685 (0.040685×100) and divided by the weight of the salt taken, will express the per cent. of zinc oxide represented in the sample.

Impure native zinc carbonate, contaminated with iron, is known in commerce as calamine, and was at one time largely used in the preparation of Turner's Cerate (calamine 3 parts, yellow wax 3 parts, lard 16 parts).

Zinc Chloride. $ZnCl_2$.—This salt may be obtained by evaporating the official solution of zinc chloride to dryness, with constant stirring, adding toward the close of the operation a little hydrochloric acid to avoid, as far as possible, the formation of oxychloride. Owing to the very hygroscopic character of the salt, it must be transferred while still warm to perfectly dry bottles, which should be closed with paraffined glass stoppers.

The entire absence of basic salt in zinc chloride is scarcely possible, and the Pharmacopœia prescribes the limit by directing that 1 drop of hydrochloric acid shall clear up the opacity caused in 5 mils. (or Cc.) of a 5 per cent. aqueous solution of the salt by the addition of an equal volume of alcohol. If flocculi are observed in a solution of zinc chloride, they are evidence of the presence of oxychloride, and should be removed by the cautious addition, drop by drop, of dilute hydrochloric acid. As zinc chloride acts destructively upon vegetable fiber, strong solutions of it should always be filtered through asbestos or glass wool.

The Pharmacopœia demands that the official salt shall contain not less than 95 per cent. of pure zinc chloride, adding to a solution of an accurately weighed quantity of the salt an excess of tenth-normal silver nitrate solution and ascertaining the excess of silver nitrate solution by titration with tenth-normal potassium sulphocyanate solution. The equation $ZnCl_2 + 2AgNO_3 = 2AgCl + Zn(NO_3)_2$ shows that 1 molecule, or 136.29 Gms., of pure zinc chloride requires 2 molecules, or 339.78 Gms., of silver nitrate for complete precipitation and hence each mil. (or Cc.) of the tenth-normal solution consumed in the official assay and containing 0.0016989 Gm. of silver nitrate corresponds to 0.0068145 Gm. of zinc chloride.

Zinc chloride may also be assayed electrolytically by determining the amount of zinc present, in the manner described under Zinc on page 679. Each Gm. of metallic zinc thus determined corresponds to 2.0849 Gms. of $ZnCl_2$.

Zinc Oxide. ZnO.—For pharmaceutical purposes zinc oxide is usually obtained by heating precipitated zinc carbonate in a crucible until all carbon dioxide and water have been expelled, the process being identical with that for the production of magnesia; thus $2ZnCO_3 + 3Zn(OH)_2 = 5ZnO + 2CO_2 + 3H_2O$. A red heat is not necessary, decomposition taking place at a temperature of 250° to 280° C. (482° to 536° F.). The lower the temperature employed for expelling the carbon dioxide the whiter will be the oxide obtained, a full red heat always causing a decided yellow tint.

The Pharmacopœia demands that the official zinc oxide shall contain, when freshly ignited, not less than 99 per cent. of pure ZnO, which is determined by dissolving an accurately weighed quantity of the freshly ignited sample in an excess of normal sulphuric acid and titrating the excess of acid with normal potassium hydroxide solution; each mil. (or Cc.) of normal acid consumed in the official assay corresponds to 0.040685 Gm. of pure zinc oxide.

Zinc oxide may also be assayed electrolytically by determining the amount of zinc present, in the manner described under Zinc on page 679. Each Gm. of metallic zinc thus determined corresponds to 1.2448 Gms. of ZnO.

Zinc oxide is occasionally designated as *flores zinci* (flowers of zinc), *nihil album* (white nothing), or *lana philosophica* (philosopher's

wool), and an impure gray variety was formerly used under the name *tutia* or *tutty*.

Zinc Phenolsulphonate. $Zn(C_6H_5O_4S)_2 + 8H_2O$ or $Zn(SO_3C_6H_4OH)_2 + 8H_2O$.—This salt, commercially better known as zinc sulphocarbolate, may be prepared by mutual decomposition between solutions of barium or lead phenolsulphonate (see Sodium Phenolsulphonate) and zinc sulphate, filtering the mixture, evaporating the clear solution, and allowing it to crystallize. When freshly prepared the crystals of zinc phenolsulphonate are colorless, but are apt to become pink upon exposure to air and light, and should therefore be preserved in small tightly stoppered amber-colored bottles. The salt effloresces when exposed to the air.

The Pharmacopœia requires that the official salt shall contain not less than 73.7 per cent. nor more than 77.4 per cent. of pure anhydrous zinc phenolsulphonate, corresponding to not less than 99.5 per cent. of the crystallized salt, which is determined as zinc oxide in the same manner as directed for the assay of zinc acetate on page 679. Since zinc phenolsulphonate contains 25.93+ per cent. of water of crystallization and 1 molecule, or 555.72 Gms., of the salt is capable of yielding 1 molecule, or 81.37 Gms., of zinc oxide, 1 Gm. of the latter must correspond to 5.05827+ Gms. of anhydrous or 6.82954+ Gms. of crystallized zinc phenolsulphonate. Each Gm. of zinc phenolsulphonate should yield not less than 0.146 Gm. nor more than 0.153 Gm. of zinc oxide to meet the official requirements.

Zinc phenolsulphonate may also be assayed electrolytically by determining the amount of zinc present, in the manner described under Zinc on page 679. Each Gm. of metallic zinc thus determined corresponds to 8.5011 Gms. of $Zn(C_6H_5SO_4)_2 + 8H_2O$.

Zinc Stearate.—This compound, which is always accompanied by small but varying proportions of zinc palmitate, may be obtained by mutual decomposition between solutions of either zinc acetate or sulphate and sodium stearate, the latter being employed hot because the salt is not very soluble in cold water. 100 parts of zinc acetate or 131 parts of zinc sulphate will require 279 parts of sodium stearate; the latter may be procured in an impure form as animal or curd soap, or be prepared of purer quality by adding stearic acid to a hot solution of monohydrated sodium carbonate. The precipitated zinc stearate, after having been thoroughly washed with hot water, is dried between bibulous paper, reduced to powder, and passed through a hair cloth sieve.

Zinc stearate has been found to retain its pulverulent condition very much better than zinc oleate, which was at one time much used and was often found mixed with zinc oxide for the purpose of better preservation.

The Pharmacopœia requires that the official salt shall contain an

amount of zinc in combination corresponding to not less than 13 per cent. nor more than 15.5 per cent. of zinc oxide, which is determined by boiling an accurately weighed quantity of the compound with an excess of tenth-normal sulphuric acid for 10 minutes; after cooling, the excess of acid is titrated with tenth-normal potassium hydroxide solution, using methyl orange as indicator. Each mil. (or Cc.) of the tenth-normal acid consumed corresponds to 0.0040685 Gm. of zinc oxide, and each Gm. of zinc stearate taken for the official assay should therefore require not less than 31 nor more than 38.1 mils. (or Cc.) of tenth-normal sulphuric acid for complete decomposition. An excessive amount of tenth-normal acid required would indicate the probable admixture of zinc oxide.

The name zinc oleostearate is applied by the British Pharmacopœia to a similar preparation, made by adding a solution of zinc sulphate to a solution of olive oil soap and animal soap; it is a mixture of zinc oleate and zinc stearate, and occurs in powder form.

Zinc Sulphate. $ZnSO_4 + 7H_2O$.—This salt is manufactured on a large scale by digesting metallic zinc with diluted sulphuric acid, when zinc sulphate is formed and hydrogen eliminated. As iron is generally present in zinc, this also is dissolved, and is removed by first converting it into a ferric salt (by passing chlorine into the solution) and afterward adding zinc carbonate, whereby all iron is precipitated as ferric hydroxide. The solution of zinc sulphate is separated by filtration, concentrated, and allowed to crystallize.

Commercial zinc sulphate frequently contains free acid, and is usually contaminated with iron and other metals; for pharmaceutical purposes only the purified salt in small crystalline granules should be used. On account of the acid reaction of an aqueous solution of zinc sulphate with litmus paper, free acid to be detected must be extracted with alcohol, which has no effect on the salt, or may be tested for in an aqueous solution of the salt with methyl orange solution, when no pink color should be developed, as directed in the Pharmacopœia.

The Pharmacopœia requires that the official salt shall contain not less than 55.86 per cent., nor more than 58.65 per cent. of pure anhydrous zinc sulphate, corresponding to not less than 99.5 per cent. of the crystallized salt, which is determined as zinc oxide in the same manner as directed for the assay of zinc acetate on page 679. Since crystallized zinc sulphate contains 43.85 per cent. of water of crystallization, each molecule, or 287.55 Gms., of the salt will yield 1 molecule, or 161.44 Gms., of anhydrous salt, capable of yielding 1 molecule, or 81.37 Gms., of pure zinc oxide; hence 1 Gm. of the latter corresponds to 1.98402 Gms. of anhydrous or 3.5338 Gms. of crystallized zinc sulphate. Each Gm. of the salt used in the official assay must yield not less than 0.2815 nor more than 0.2955 Gm. of zinc oxide in order to fulfil the official requirements.

Zinc sulphate may also be assayed electrolytically by determining the amount of zinc present, in the manner described under Zinc on page 679. Each Gm. of metallic zinc thus determined corresponds to 4.3988 Gms. of $ZnSO_4 + 7H_2O$.

Zinc Valerate. $Zn(C_5H_9O_2)_2 + 2H_2O$ + or $(CH_3)_2CHCH_2COO)_2Zn + 2H_2O$.—Formerly officially, and commercially still, named Zinc Valerianate. When hot solutions of sodium valerate and zinc sulphate are mixed, double decomposition takes place, sodium sulphate and zinc valerate being produced, the former of which remains in solution, while a portion of the zinc salt separates in the form of scaly crystals and rises to the surface; a further yield of crystals may be obtained upon concentration of the mother-liquor. The crystals are afterward drained, washed with small quantities of cold water, and dried at ordinary temperature.

The Pharmacopœia requires that the official salt shall contain not less than 99 per cent. of crystallized zinc valerate, which is determined as zinc oxide by dissolving an accurately weighed quantity of the salt in water with the aid of a few drops of hydrochloric acid if necessary, and then proceeding as directed for the assay of zinc acetate on page 679. Since each molecule, or 303.55 Gms., of zinc valerate is capable of yielding 1 molecule, or 81.37 Gms., of zinc oxide, 1 Gm. of the latter must correspond to 3.7304 Gms. of crystallized zinc valerate.

Zinc valerate may also be assayed electrolytically by determining the amount of zinc present, in the manner described under Zinc on page 679. Each Gm. of metallic zinc thus determined corresponds to 4.6436 Gms. of $Zn(C_5H_9O_2)_2 + 2H_2O$.

Solution of Zinc Chloride.—An aqueous solution of zinc chloride, $ZnCl_2$, containing about 50 per cent. of the anhydrous salt. The official directions for preparing this solution are to digest granulated metallic zinc with moderately diluted hydrochloric acid until the acid is saturated; the solution is decanted, and after the addition of a small quantity of nitric acid heated at a temperature not exceeding 115° C. (239° F.) until a portion, if removed and cooled, solidifies. It is then allowed to cool and the solidified mass is dissolved in sufficient water to bring the weight of the solution up to 1000 Gms. for every 840 Gms. of hydrochloric acid and 240 Gms. of zinc employed. Finally some zinc carbonate is added, the mixture agitated occasionally during twenty-four hours, allowed to settle, and the liquor decanted.

The object of adding nitric acid to the solution is to convert any iron present (derived from the zinc) into ferric chloride. To remove any nitrogen compounds or nitrate formed, the liquid is further evaporated to the solidifying point at a temperature below 115° C. (239° F.), so as to avoid volatilization of any zinc chloride. The final addition of zinc carbonate precipitates all iron as ferric hydroxide, and thus a solution of zinc chloride only is obtained.

Solution of zinc chloride has a specific gravity of about 1.548 at 25° C. (77° F.), and is chiefly used for disinfecting purposes. It is practically identical with Burnett's disinfecting fluid.

The Pharmacopœia requires that solution of zinc chloride shall contain not less than 49 per cent. nor more than 51 per cent. of pure zinc chloride, which is determined by adding to an accurately weighed amount of the solution an excess of tenth-normal silver nitrate solution and then titrating the excess of silver nitrate solution with tenth-normal potassium sulphocyanate solution, as explained under Zinc Chloride on page 681. As each mil. (or Cc.) of tenth-normal silver nitrate solution corresponds to 0.0068145 Gm. of pure zinc chloride, the number of mils. (or Cc.) consumed in the official assay, when multiplied by 0.68145 (0.0068145 × 100) and then divided by the weight of solution of zinc chloride taken, will express the per cent. of pure $ZnCl_2$ present in the sample.

Besides the foregoing compounds of zinc the following are of interest:

Zinc Phosphide. Zn_3P_2.—Phosphorus and zinc may be made to unite by carefully adding small pieces of the former to fused zinc contained in a crucible, but it is difficult to obtain a product of uniform composition. A more desirable method for preparing the compound is that of Proust, whereby a mixture of hydrogen phosphide and nitrogen is passed into a porcelain tube containing metallic zinc heated to redness, the metal combining with the phosphorus, while the nitrogen and liberated hydrogen escape.

Zinc phosphide must be preserved in tightly stoppered vials, as upon exposure to air it slowly emits phosphorus vapor, indicating decomposition and oxidation.

Zinc Salicylate. $Zn(C_7H_5O_3)_2 + 3H_2O$ or $C_6H_4(OH)COO)_2Zn + 3H_2O$.—This salt may be conveniently obtained by gradually adding to a hot mixture of salicylic acid and water an aqueous suspension of zinc oxide as long as solution is effected, which is then filtered and allowed to crystallize.

THE COMPOUNDS OF GOLD.

Gold and Sodium Chloride.—The official preparation is not a true double salt of the same name, but a mixture of gold chloride and sodium chloride. The double chloride of gold and sodium, known also as sodium chloroaurate, contains about 76 per cent. of pure auric chloride, whereas the official compound contains but 50 per cent. The exact composition of commercial gold and sodium chloride depends upon the mode of preparation; a simple mechanical mixture made by triturating sodium and gold chlorides together in equal proportions would be in conformity with the official definition.

Anhydrous auric chloride, $AuCl_3$, may be prepared by dissolving gold in nitromuriatic acid, evaporating the solution to dryness, dissolving the residue in water, and carefully evaporating the liquid to dryness at a temperature not exceeding 150° C. (302° F.); this operation is necessary to free the salt from acid, but a higher temperature must be avoided, lest decomposition of the auric chloride into aurous chloride and chlorine occur.

A solution of metallic gold in a mixture of nitric and hydrochloric acids contains chloroauric acid, according to the equation $Au_2 + 2HNO_3 + 8HCl = 2HAuCl_4$ or $2(AuCl_3 + HCl) + 2NO + 3H_2O$, and by adding to such a solution sodium chloride the double salt, sodium chloroaurate, is obtained upon evaporation; thus, $HAuCl_4 + NaCl = NaAuCl_4$ or $(AuCl_3 + NaCl) + HCl$. For the formation of this compound 5.187 parts of auric chloride require 1 part of sodium chloride; hence if equal parts of the two salts are used, a large excess of sodium chloride will be present.

The Pharmacopœia requires that the official compound, when dried to constant weight in a desiccator over sulphuric acid, shall contain an amount of gold chloride representing at least 30 per cent. of metallic gold, which is determined by adding an excess of potassium hydroxide solution to a solution of 0.5 Gm. of gold and sodium chloride, previously dried to constant weight, adding hydrogen dioxide solution, and heating the mixture for an hour on a waterbath. The precipitated metallic gold is well washed with water acidulated with hydrochloric acid, dried and ignited, and should then weigh not less than 0.15 Gm., which corresponds to at least 30 per cent. of the 0.5 Gm. taken. The reactions involved in the test may be indicated by the following equations: $2AuCl_3 + 12KOH = 2K_3AuO_3 + 6KCl + 6H_2O$ and $2K_3AuO_3 + 3H_2O_2 = 2Au + 3O_2 + 6KOH$.

Gold chloride being readily reduced by contact with organic matter, all such mixtures should be avoided; and as the official preparation is chiefly used in pill form, non-oxidizable excipients only should be employed (see also page 399).

THE COMPOUNDS OF SILVER.

Silver Nitrate. $AgNO_3$.—This salt is preferably made from pure silver, and in order to obtain a product free from acid the metal is dissolved in nitric acid, the solution evaporated to dryness, the residue fused and redissolved in water, the solution filtered and allowed to crystallize. The evaporation to dryness and fusion of the residue are for the purpose of expelling any uncombined acid present, which, if the first solution were allowed to crystallize would to some extent be retained mechanically within the crystals: a temperature exceeding 200° C. (392° F.) must, however, be avoided, lest some of the silver nitrate be reduced to nitrite.

Silver nitrate is easily decomposed by contact with organic matter,

and when exposed to light gradually assumes a gray color; hence proper precautions must be observed in keeping and dispensing it.

The Pharmacopœia requires almost absolute purity for this salt by demanding that when finely powdered and dried to constant weight in a desiccator over sulphuric acid, in the dark, it shall contain not less than 99.8 per cent. of pure silver nitrate, which is determined by titrating an accurately weighed quantity of the previously dried salt, dissolved in distilled water, in the presence of nitric acid, with tenth-normal potassium sulphocyanate solution, each mil. (or Cc.) of which corresponds to 0.016989 Gm. of $AgNO_3$.

Moulded Silver Nitrate.—Under this name the Pharmacopœia recognizes a mixture of silver nitrate and chloride, containing about 5 per cent. of the latter salt, and prepared by adding 1 part of hydrochloric acid to 25 parts of pure silver nitrate, melting the mixture at as low a temperature as possible and casting the mass in moulds. The object of converting a part of the silver nitrate into chloride is to render the resulting mass less brittle.

The synonym *lunar caustic*, given to this preparation in the U. S. Pharmacopœia, does not correspond with the same term commercially, which is usually applied to pure silver nitrate moulded into sticks, as also indicated in the British Pharmacopœia. The latter authority applies the name *toughened caustic* (argenti nitras induratus) to a mixture of 95 parts of silver nitrate and 5 parts of potassium nitrate.

The Pharmacopœia requires that moulded silver nitrate shall contain not less than 94.5 per cent. of pure silver nitrate, which is determined by titrating a solution of the compound, from which the silver chloride has been removed by filtration, with tenth-normal potassium sulphocyanate solution in the same manner as directed for the assay of silver nitrate.

Silver Oxide. Ag_2O.—This compound may be obtained by adding a solution of pure silver nitrate to a solution of potassium or sodium hydroxide, washing the resulting precipitate well with water, and finally drying the same on a waterbath. Ammonia water is not suitable for the process, since it forms a soluble compound with the oxide, having the composition $Ag_2O + NH_3$.

The Pharmacopœia requires that this compound, when dried to constant weight at 120° C. (248° F.), shall contain not less than 99.6 per cent. of pure silver oxide, which is determined by dissolving an accurately weighed quantity of the previously dried compound in a mixture of nitric acid and water and then titrating this solution with tenth-normal potassium sulphocyanate solution in the manner directed for the assay of silver nitrate. Each mil. (or Cc.) of the tenth-normal potassium sulphocyanate solution required corresponds to 0.011588 Gm. of pure Ag_2O.

Silver oxide is rarely employed in medicine at the present time, and

should always be kept in dark amber-colored bottles to avoid reduction. It is quickly decomposed by oxidizing agents, and should never be triturated with organic substances.

THE COMPOUNDS OF URANIUM.

Uranium Nitrate. $UO_2(NO_3)_2 + 6H_2O$.—This salt appears for the first time in our Pharmacopœia and is not officially recognized in other countries. It is obtained almost wholly from the mineral known as pitchblende, the chief constituent of which is uranoso-uranic oxide, U_3O_8 or $UO_2\ 2UO_3$. The ore is first roasted to get rid of arsenic and sulphur, and is then ground and washed with diluted hydrochloric acid in which the uranium oxide is insoluble; the residue is finally dissolved in nitric acid, converting the oxide into uranium nitrate. In order to further purify the salt, hydrogen sulphide may be passed through a solution of uranium nitrate, whereby any lead, arsenic, tin and other metals still remaining will be precipitated; after filtration the liquid is then evaporated with nitric acid and allowed to crystallize.

Uranium nitrate occurs in the form of light yellow prisms, odorless and having a bitter, astringent taste; it is somewhat efflorescent and radio-active. It is soluble in a little more than its own weight of water, and is freely soluble in alcohol and ether. Aqueous solutions of the salt are yellow in color and acid to litmus.

The Pharmacopœia requires that uranium nitrate shall contain not less than 98 per cent. of uranyl nitrate, which is determined by adding ammonia water to a boiling aqueous solution of an accurately weighed quantity of the salt until no further precipitation is produced. The precipitate is well washed with an aqueous 1 per cent. solution of ammonium nitrate and then moderately ignited in a crucible, with free access of air, to constant weight. The urano-uranic oxide, thus obtained should correspond to not less than 54.8 per cent. of the weight of the salt taken, which is equivalent to not less than 98 per cent. of crystallized uranyl nitrate.

ORGANIC SUBSTANCES.

UNDER this head are classified those many compounds of carbon, hydrogen, and oxygen, frequently associated with nitrogen, sulphur, phosphorus, and other elements, which are chiefly derived from the vegetable kingdom; a few are obtained also from the animal kingdom, and some are produced synthetically.

Prior to 1828, when Woehler announced to the scientific world the successful synthetic production of urea, an excretory product of the animal economy, solely from inorganic material, thereby establishing the intimate relationship between organic and inorganic matter, the agency of a peculiar vitalizing force was considered essential for the formation of all so-called organic bodies. No elements unknown to the mineral kingdom have ever been found in organic bodies, and the one feature which serves to distinguish this very large class of chemical compounds from those commonly designated as inorganic substances is the invariable presence of carbon; the term carbon compounds is therefore most appropriately applied to them.

The simplest form of carbon compounds are the hydrocarbons, composed exclusively of carbon and hydrogen; of these, two, methane, CH_4, and benzene, C_6H_6, may be said to be the source of all organic compounds, the constitution of which has thus far been studied and explained. The derivatives of these two hydrocarbons differ so widely in their properties that they have been conveniently grouped into two main classes, designated as fatty and aromatic compounds, respectively.

It is not within the scope of this book to enter into a detailed study of the so-called organic substances, and attention will be given only to those of pharmaceutical interest.

CHAPTER LIII.

CELLULOSE AND ITS DERIVATIVES.

ALL plants are made up of certain proximate principles, to which they owe their growth and value as nourishing or medicinal agents. The most widely diffused substance in the vegetable kingdom is cellulose or cell membrane, which goes to make up the body of all plants. During the growth and development of plants some of the cell membrane undergoes a change, becoming gradually hard and woody; to this modified form of cellulose the name lignin has been given, and the woody fiber of plants is assumed to be a combination of cellulose and lignin, called lignose. Cellulose and lignin being insoluble in all ordinary solvents, the chief object in pharmaceutical processes is to extract from them, by appropriate treatment, the many valuable principles they often enclose and upon which the medicinal value of vegetable drugs depends.

Lignin has not yet been obtained in a pure state, but pure cellulose has been isolated as a colorless, odorless, and tasteless gelatinous mass, which, upon drying, forms a horny substance, or may be obtained as a white powder. It is soluble in a solution of cupric hydroxide in ammonia water, known as Schweitzer's reagent, forming a mucilaginous fluid which, after dilution, admits of filtration, and, upon addition of an acid, is again precipitated. The elementary composition of pure cellulose corresponds to the formula $C_6H_{10}O_5$, or multiples thereof, as $C_{12}H_{20}O_{10}$ or $C_{18}H_{30}O_{15}$.

Cellulose is officially recognized in the form of gossypium, or cotton, and patent lint and paper are further examples of it. When heated with potassium or sodium hydroxide it is gradually converted into oxalic acid, alkali oxalates being formed, and, if boiled with diluted sulphuric acid, dextrin is produced, which is finally changed into dextrose, from which alcohol can be obtained by fermentation. Immersed in strong sulphuric acid, cellulose undergoes conversion into a substance called amyloid, upon which the preparation of parchment paper depends, the pores of the paper becoming filled with this modified cellulose, and thus made tough and impervious to water. Prolonged contact of the paper with strong sulphuric acid, however, is hurtful, the resulting product becoming friable; hence the best results are obtained if the paper be simply drawn through a mixture of two parts of concentrated sulphuric acid and one part of water, and then immediately well washed with water.

Official purified cotton, commercially known as absorbent cotton, is prepared by first boiling carefully carded cotton in a weak alkaline

solution, for the purpose of removing fatty matter, after which it is rinsed in water and immersed in a weak solution of chlorinated lime. It is subsequently washed in water slightly acidulated with hydrochloric acid, and again well rinsed in water. If the cotton still retains fat, the treatment with alkali is repeated until the final product is found completely absorbent. For the more thorough removal of water after washing the cotton recourse is had to centrifugal machines, by means of which the material is rapidly dried.

Medicated cotton is usually prepared by impregnating absorbent cotton with a solution of the medicinal agent in alcohol and glycerin, and subsequently drying; the glycerin not being volatilized, serves as an adhesive agent for retaining the active ingredient on the fiber of the cotton. The solution is used of a definite strength and in such quantity that the whole of it will be absorbed by and saturate the material. Benzoated, borated, carbolated, iodized, salicylated, and other medicated cotton is prepared in this or a similar manner. The percentage of medicinal agent present must be calculated on the basis of finished product, irrespective of any adhesive agent that may have been employed, and which naturally forms a part of the finished product; thus, 25 Gms. of 10 per cent. borated cotton should contain 2.5 Gms. of boric acid, or 10 Gms. of 5 per cent. carbolated cotton should contain 0.5 Gm. of pure carbolic acid, etc. It has been suggested that impregnation of cotton with a 5 or 10 per cent. solution of any medicinal agent would constitute such cotton a 5 or 10 per cent. medication; but such an assumption is erroneous, since the absolute quantity of medicinal agent retained by the cotton must always be uncertain and variable in its relation to the weight of the finished product.

Cellulose and lignose both furnish most valuable pharmaceutical derivative products, the former by appropriate treatment with nitric acid, and the latter by dry distillation.

Pyroxylin.—Under this name the United States and British Pharmacopœias recognize a compound soluble in a mixture of alcohol and ether, and better known as collodion cotton or soluble gun cotton, since it is used extensively in the preparation of collodion; the name colloxylin is also used as a synonym in this country. In Continental Europe the two terms are not considered synonymous, the name pyroxylin being applied to insoluble gun cotton, and colloxylin to soluble collodion cotton. Pyroxylin is usually prepared by macerating purified cotton in a cooled mixture of 14 volumes of nitric acid and 22 volumes of sulphuric acid until the cotton has become soluble in a mixture of 1 volume of alcohol and 3 volumes of ether, then removing all adhering acid by washing first with cold and then with boiling water, and finally drying the product in small portions at a moderate heat (60° C. (140° F.)).

When cotton is thoroughly imbued with strong nitric acid, cellulose

nitrates and water are formed; thus, $C_6H_{10}O_5 + 2HNO_3 = C_6H_8(NO_3)_2O_3 + 2H_2O$. The exact character of the reaction depends upon the strength of the acid used, the temperature at which the cotton is immersed, and the length of time maceration is continued; thus, di-, tri-, tetra, penta-, and hexanitrate may be produced. The last two compounds are insoluble in alcohol and ether, and hence unfit for the purposes of official pyroxylin, which latter probably consists chiefly of cellulose tetranitrate, $C_{12}H_{16}(ONO_2)_4O_6$. It is important that the acids used be of official strength, and that the acid mixture, which becomes heated, be allowed to cool to 32° C. (90° F.) before the cotton is added, otherwise, in the latter case, the higher nitrates are formed and the staple of the cotton is destroyed; if weak acids be employed, prolonged maceration becomes necessary and imperfect nitration may result; in either case the product is insoluble.

In order that the cotton may be completely saturated with the acid mixture, it should be introduced in small portions by the aid of a glass rod. The sulphuric acid used takes no part in the reaction, but facilitates the same by absorbing the water which is eliminated.

The Pharmacopœia requires that pyroxylin shall not yield more than 0.075 per cent. of its weight to distilled water, when shaken with the latter (limit of soluble impurities), and when saturated with alcohol and then ignited, it shall not leave more than 0.3 per cent. of ash.

Pyroxylin was at one time looked upon as a nitro substitution compound, and called nitrocellulose, the group NO_2 having been supposed to replace hydrogen in cellulose. Further studies of cellulose and the behavior of pyroxylin toward reagents have shown the latter compound to be a nitric acid ester or compound ether, formed by the displacement of hydrogen in the hydroxyl groups by the nitric acid radical, as shown by the formula $C_6H_8(ONO_2)_2O_3$ or $C_6H_7(ONO_2)_3O_2$. The correctness of this view is shown by the fact that nitric acid can be abstracted from cellulose nitrates by treatment with alkalies, and can also be completely displaced by concentrated sulphuric acid, even in the cold. All cellulose nitrates can be converted back into cellulose by reducing agents, and the degree of nitration can be definitely determined by treatment with ferrous sulphate and hydrochloric acid, the nitric oxide liberated being collected in a graduated tube, and from this the amount of nitric acid present can be calculated; the following equation explains the reaction: $2C_6H_7(ONO_2)_3O_2 + 18HCl + 18FeSO_4 = 2C_6H_{10}O_5 + 6NO + 6Fe_2(SO_4)_3 + 3FeCl_6 + 6H_2O$.

Pyroxylin is used in pharmacy exclusively in the preparation of plain and medicated collodion (see page 360), but has met with more extensive application in the arts in the manufacture of celluloid, a mixture of pyroxylin and camphor.

The Products of Distillation.—When wood is subjected to heat in air-tight cylinders or retorts a number of new substances are

obtained, as a result of destructive distillation, the character of which depends largely upon the degree of heat employed and the care with which the process has been conducted. Both liquid and gaseous products are formed and distil over, when the solid residue is either charcoal or the original wood employed, but slightly altered in appearance. The liquid distillates include an acid fluid and tar; the former is known as pyroligneous acid or wood vinegar, which contains, besides acetic acid, acetone, C_3H_6O, methyl or wood alcohol, CH_3OH, furfurol, $C_5H_4O_2$, catechol or pyrocatechin, $C_6H_4(OH)_2$, and other substances.

Pyroligenous acid is not recognized in our Pharmacopœia, but is official in the German Pharmacopœia as *Acetum Pyrolignosum*, both the crude and rectified varieties being named. The former is described as a brown liquid containing at least 6 per cent. of acetic acid, and the latter as a yellowish liquid containing at least 5 per cent. of acetic acid; both liquids have a decided empyreumatic odor.

Acetic Acid. $HC_2H_3O_2$ or CH_3COOH.—Although acetic acid can be produced by oxidation of weak alcoholic liquids, it is obtained for the trade indirectly from wood.

Formerly much acetic acid was obtained in the form of wood vinegar or pyroligneous acid, by destructive distillation of oak wood in large iron retorts kept at a temperature of 205° C. (401° F.). This crude acid liquid, of slight yellowish color, was neutralized with soda-ash or sodium carbonate and evaporated, the resulting sodium acetate being then roasted to destroy empyreumatic products and to drive off water and other volatile matter. Upon finally treating the sodium acetate in suitable stills with sulphuric acid, purified acetic acid was obtained. This plan has, however, been abandoned by manufacturers, who now prefer to procure the acetic acid in the form of calcium acetate from charcoal burners, and then bring this into solution and decompose it with sodium sulphate, whereby calcium sulphate is precipitated and sodium acetate remains in solution, which is then filtered and further treated as above explained.

If wood is distilled at temperatures above 230° C. (446° F.), as in the manufacture of charcoal, the resulting wood vinegar is more or less highly colored and possesses a strong empyreumatic odor. It requires a tedious process of purification by means of milk of lime, whereby soluble calcium acetate is formed and many impurities are precipitated as insoluble calcium compounds.

Chemically, acetic acid may be looked upon as methane or marsh gas (CH_4), in which an atom of hydrogen has been replaced by the carboxyl group, COOH, forming a monobasic acid; thus, $CH_3COOH = HC_2H_3O_2$. It is a remarkably stable acid, and, although rich in oxygen, is not decomposed at moderately high temperatures, nor is it readily affected by oxidizing or reducing agents.

The Pharmacopœia recognizes three grades of acetic acid, which

are officially designated as glacial acetic acid, acetic acid, and diluted acetic acid, and contain, respectively, 99, 36, and 6 per cent. of absolute $HC_2H_3O_2$. The three acids, recognized by the same names in the British Pharmacopœia, correspond very closely in strength to the above, containing 98.9, 33, and 5 per cent. of absolute acetic acid, respectively; but in the German Pharmacopœia the term acetic acid is used to designate a solution containing 96 per cent. of absolute acid, while the German diluted acetic acid contains 30 per cent.

Specific gravity is of no value in the examination of acetic acid, since the maximum density is reached in an 80 per cent. solution; beyond this point the specific gravity again decreases until absolute acetic acid is reached, having a density of 1.053. Official glacial acetic acid and an acid of 46 per cent. have the same specific gravity, 1.058, at 15° C. (59° F.), and, if diluted with water, the density of the weaker acid only will fall, that of the stronger acid increasing; between 73 and 84 per cent. acetic acid the specific gravity is almost stationary, the rise between these two points amounting to not more than 0.0008. Titration with normal alkali solution, as directed in the Pharmacopœia, is the only correct means of ascertaining the strength of acetic acid solutions, each mil. (or Cc.) of normal potassium hydroxide solution corresponding to 0.06003 Gm of absolute $HC_2H_3O_2$, as shown by the equation $KOH + HC_2H_3O_2 = KC_2H_3O_2 + H_2O$.

Glacial acetic acid is obtained by distilling anhydrous sodium acetate with highly concentrated sulphuric acid and exposing the resulting liquid to a temperature below 10° C. (50° F.); after crystallization has taken place the remaining liquid may be drained off and again exposed to cold to secure a further yield of crystals. Glacial acetic acid should contain not less than 99 per cent. of pure hydrogen acetate or absolute acetic acid and should retain its crystalline form until a temperature of at least 15° C. (59° F.) is reached, when it slowly begins to liquefy; some of the so-called glacial acetic acid of commerce is simply a strong solution, containing from 75 to 85 per cent. of absolute acid, and does not solidify at a temperature of 5° C. (41° F.) or even lower.

Glacial acetic acid readily absorbs moisture from the air and must therefore be preserved in tightly stoppered bottles. At ordinary room temperature it is a colorless liquid, but when the temperature falls below 15° C. (59° F.) it congeals to a crystalline mass and remains in that condition during cold weather. It has been employed as an excellent solvent for certain volatile oils, resins, and fatty bodies.

Official acetic acid is obtained, like the glacial acid, by distilling sodium acetate with sulphuric acid and finally adjusting the strength to the requirements of the Pharmacopœia. It should contain not less than 36 per cent. nor more than 37 per cent. of absolute acetic acid, and is used in pharmacy chiefly for the preparation of the official diluted acid, and also as an addition to the menstruum employed for tincture of sanguinaria and several extracts and fluidextracts.

Acetic acid for pharmaceutical purposes should be free from empyreuma, which may be detected by means of potassium permanganate, the color of which is readily discharged by empyreumatic substances. Upon neutralizing the acid with alkali and warming, no foreign odor should be perceptible.

Pharmacists will find it to their interest to purchase strong acetic acid and dilute this to suit their requirements, according to the rule given on page 134. Acetic acid of 60 and 80 per cent. strength can be purchased from reliable manufacturers at a relatively lower price than the official acid.

The commercial variety of acetic acid known as "No. 8" should never be used in place of the official acid, as it is weaker, containing only about 30 per cent. of absolute acid.

Diluted acetic acid, recommended in the Pharmacopœia in place of commercial vinegar as a menstruum for several official preparations, is made by mixing 12 parts by weight of the 36 per cent. acid with 61 parts by weight of distilled water, and should contain not less than 5.8 per cent. nor more than 6.3 per cent. of absolute $HC_2H_3O_2$. Its advantages over ordinary vinegar are purity and uniformity of strength, besides which the entire absence of color enables it to be used for colorless solutions, such as Spirit of Mindererus and the like.

Trichloracetic Acid. $HC_2Cl_3O_2$ or CCl_3COOH.—When chlorine is allowed to act on acetic acid, mono-, di-, and tri- substitution compounds are formed. The latter, known as trichloracetic acid, is official in the U. S. Pharmacopœia. It may be prepared by adding fuming nitric acid to fused hydrated chloral and setting the mixture aside until red vapors cease to be formed, after which it is distilled, that portion coming over above 190° C. (374° F.) and consisting of pure trichloracetic acid being collected.

Trichloracetic acid occurs in colorless deliquescent crystals, readily soluble in water, alcohol, and ether. It should be preserved in dark amber-colored, tightly stoppered bottles. When mixed with $\frac{1}{10}$ its weight of water it forms a permanently liquid mixture. The acid is used as a cauterizing agent in minor surgery, but never employed internally.

Among the substances associated with acetic acid in crude wood vinegar are two of greater interest to pharmacists than the rest—acetone and methyl alcohol.

Acetone. C_3H_6O or CH_3COCH_3.—This compound, at one time also known as pyroacetic ether or pyroacetic spirit, was formerly obtained on a commercial scale solely by the destructive distillation of acetates (chiefly calcium acetate), but in 1895 a process was devised by the late Dr. E. R. Squibb for decomposing acetic acid vapor at a high temperature, between 500° and 600° C. (932° and 1112° F.),

in a specially constructed iron rotary apparatus, whereby a large yield of fairly pure acetone may be secured. The crude acetone thus obtained is afterward purified by dehydration with caustic lime and redistillation. The decomposition of acetic acid vapor results in the formation of acetone and carbon dioxide, with the liberation of water; thus, $2HC_2H_3O_2 = C_3H_6O + CO_2 + H_2O$. The process and apparatus are fully described in *Ephemeris*, vol. iv., No. 3.

Chemically, acetone belongs to the class of compounds known as ketones, which consist of two alcohol radicals united by means of the bivalent group CO, called carbonyl; hence acetone is called also dimethyl ketone, and may be looked upon as acetic aldehyde, CH_3COH, in which a hydrogen atom is replaced by the methyl group.

Acetone is now extensively employed for the manufacture of chloroform, iodoform, etc., and has been found a valuable solvent for oleoresins, collodion cotton, etc. When pure it is a colorless, mobile, inflammable liquid of 0.790 specific gravity at 25° C. (77° F.), and boiling between 56° and 58° C. (132.8° and 136.4° F.). It is miscible in all proportions with water and alcohol, hence the commercial article is sometimes found contaminated with these substances.

The Pharmacopœia requires that acetone shall contain not less than 99 per cent. of dimethyl ketone, which is determined by ascertaining the quantity of tenth-normal iodine solution required to convert a definite weight of acetone into iodoform, each mil. (or Cc.) of the iodine solution consumed corresponding to 0.0009675 Gm. of pure $CH_3.CO.CH_3$.

Several reactions occur in the official assay method, the first one resulting in the formation of tri-iodoacetone and hydriodic acid, as shown by the equation, $CH_3COCH_3 + I_6 = CI_3COCH_3 + 3HI$; the tri-iodoacetone reacts with potassium hydroxide, being converted into iodoform and potassium acetate, while the hydriodic acid is neutralized by potassium hydroxide, forming potassium iodide with elimination of water, thus, $CI_3COCH_3 + 3HI + 4KOH = CHI_3 + CH_3COOK + 3KI + 3H_2O$. At the same time the excess of iodine reacts with potassium hydroxide and forms potassium iodide and potassium iodate, which are subsequently decomposed by the hydrochloric acid, liberating iodine; the latter is finally determined by titration with sodium thiosulphate. Since 1 molecule, or 58.05 Gms., of absolute acetone requires 6 atoms, or 761.52 Gms., of iodine for reaction, it follows that each mil. (or Cc.) of tenth-normal iodine solution, containing 0.012692 Gm. of iodine, must correspond to 0.0009675 Gm. of pure acetone.

The purpose of making the blank test directed in the Pharmacopœia, is to determine whether any iodine ultimately disappears in the reaction with the potassium hydroxide used in the assay of the acetone sample. Theoretically, all the iodine that reacts with the alkali is liberated again when the solution is acidified, but practically some of the iodine may be consumed by impurities in the alkali, so that not quite as much

will be liberated upon addition of the acid as was originally added to the alkali. If in the blank test 35 mils. (or Cc.) of tenth-normal iodine solution are added to the alkali, and after acidifying, less than 35 mils. (or Cc.) of tenth-normal sodium thiosulphate solution are required to titrate the liberated iodine, the difference is the amount of iodine solution consumed by possible impurities, which must be applied as a correction in the calculation for acetone.

The apparent amount of iodine solution consumed by the acetone in the assay is the difference between the 35 mils. (or Cc.) of tenth-normal iodine solution added, and the number of mils. (or Cc.) of tenth-normal sodium thiosulphate solution required to titrate the residual iodine liberated upon addition of the hydrochloric acid. The actual amount of iodine solution consumed by the acetone is the difference between this apparent amount and the amount of iodine consumed in the blank test. This remainder in mils. (or Cc.) of tenth-normal iodine solution, when multiplied by 3.87 (0.0009675 × 40 × 100) and divided by the weight of acetone originally taken, will express the per cent. of absolute dimethyl ketone in the sample. It must be borne in mind that only one-fortieth of the original weight of acetone taken is involved in the final titration.

Among the derivatives of acetone the following is officially recognized:

Sulphonmethane. $C_7H_{16}S_2O_4$ **or** $(CH_3)_2C(SO_2C_2H_5)_2$.—Although the Pharmacopœia has, for the sake of more convenient brevity, adopted the present official title, the true chemical name of the compound is diethylsulphone-dimethylmethane. It is best known by its trade name, under which it was first introduced into medicine, *sulphonal*, and is also recognized by this name in the British and German Pharmacopœias. The first step in its manufacture is the preparation of mercaptol or dithioethyl-dimethylmethane, $(CH_3)_2C(SC_2H_5)_2$, a condensation product obtained when dry hydrochloric acid gas is passed into a mixture of anhydrous acetone and anhydrous ethyl hydrosulphide (ethyl mercaptan), water being eliminated; thus $2C_2H_5SH + CO(CH_3)_2 = (CH_3)_2C(SC_2H_5)_2 + H_2O$. Mercaptol is an oily liquid of exceedingly disagreeable odor, which may be purified by washing with water and afterward with dilute solution of sodium hydroxide. Upon agitating mercaptol with a 5 per cent. potassium permanganate solution until the color of the latter remains, oxidation takes place and sulphonmethane is formed. The new product may be obtained absolutely pure by crystallization from water or alcohol.

Sulphonmethane occurs in the form of colorless, odorless, and nearly tasteless crystals, requiring 365 parts of water for solution at 25° C. (77° F.), but is soluble in 16 parts of boiling water.

Three compounds similar to sulphonal have been introduced as hypnotics, of which one is also recognized in the Pharmacopœia, *methonal*, *tetronal*, and *trional*. Methonal is chemically dimethyl-

sulphone-dimethylmethane $(CH_3)_2C(SO_2CH_3)_2$, and tetronal is diethylsulphone-diethylmethane $(C_2H_5)_2C(SO_2C_2H_5)_2$; both are made like sulphonal, except that in the case of methonal methyl hydrosulphide is used in place of ethyl hydrosulphide, and in the case of tetronal, diethylketone is used in place of acetone. Trional is officially recognized under the name:

Sulphonethylmethane.—This compound is chemically diethylsulphone-methylethylmethane (CH_3) $(C_2H_5)C(SO_2C_2H_5)_2$, but is better known by its trade name, trional. It is made exactly like sulphonal, except that acetone is replaced by methylethylketone, $CH_3COC_2H_5$. It differs from sulphonal chiefly in having a bitter taste and in being nearly twice as soluble in cold water, requiring 200 parts for solution at 25° C. (77° F.). Sulphonethylmethane is recognized in the German Pharmacopœia as *methylsulphonal.*

Methyl Alcohol. CH_4O or CH_3OH.—This compound, also known as wood alcohol and at one time called wood naphtha and pyroxylic spirit, is obtained in a crude state from pyroligneous acid or wood vinegar, see page 693, by distillation, after neutralization with sodium carbonate or milk of lime. The wood vinegar obtained by destructive distillation of hard woods, such as beech, birch, and maple, is preferred, because the yield of methyl alcohol therefrom is higher. The yield is also influenced by the particular method of distillation of the wood; thus, a cord of hard wood distilled in ovens or retorts will yield from 8 to 10 gallons of methyl alcohol, 82 per cent. pure, while if distilled in kilns, the yield rarely exceeds from 4 to 6 gallons.

There are nearly 100 plants in the United States engaged in the production of methyl alcohol, and it is stated in government reports that the the annual production exceeds 30,000,000 gallons. The primary products are crude wood alcohol, calcium acetate and charcoal; the first named article is a very complex substance, consisting chiefly of methyl alcohol, acetone, methyl acetate, dimethyl acetal, aldehydes and ketones. By repeated fractional distillation and other refining processes the crude wood alcohol is made to yield methyl alcohol, methyl acetone, allyl compounds, wood oils and wood tar. The methyl alcohol thus obtained, which is more or less dilute, may be further purified by heating on a waterbath with an excess of anhydrous calcium chloride, whereby a crystalline compound, $CaCl_2 + 4CH_3OH$, is formed, which after all volatile matter has been dissipated is mixed with water and distilled, resulting in the recovery of methyl alcohol, to be subsequently dehydrated with lime and redistilled.

For some years purified methyl alcohol containing 97 to 98 per cent. of CH_3OH was sold under the trade-mark name *Columbian Spirit*, but this name has been changed to *Columbian Methanol* by the owners, the Wood Products Co., of Buffalo, N. Y., in order to prevent confusion between methyl or wood alcohol and ethyl or grain spirit. The name

Colonial Spirit has also been applied to wood alcohol of high grade by some manufacturers.

Methyl or wood alcohol should never be used for pharmaceutical preparations, whether for internal or external use, on account of its toxic properties. Experiments made during the past 10 or 12 years have demonstrated that methyl alcohol does not act like ordinary or grain alcohol when administered internally, being eliminated less rapidly, and frequently causing blindness and other grave functional disturbances. Even when used in place of grain alcohol for the preparation of external remedies, it has been found to act as a poison, and hence is wholly unfit for use in pharmacy and medicine and for toilet preparations. As a fuel in spirit lamps it has been preferred on account of its lesser cost; for the same reason it is used in the place of grain alcohol for the preparation of varnishes and for other technical purposes; no objections can be raised against such uses, if proper ventilation is provided for the escape of the vapors, but the inhalation of methyl alcohol vapor in closely confined spaces for any length of time has proved injurious to many persons.

Absolutely pure methyl alcohol is best prepared by distilling crystallized methyl oxalate with solution of potassium hydroxide and then dehydrating with lime; the cost of such an article is, however, two or three times as high as that of absolute ordinary or ethyl alcohol. Pure methyl alcohol boils at a comparatively low temperature, 66° C. (150.8° F.). Methyl alcohol is largely used in this country and in England and Germany for the purpose of rendering ordinary alcohol unfit for other than technical uses, by mixing the two liquids; in Germany a further addition of allyl alcohol and acetone is prescribed. Ethyl alcohol thus mixed is known in England as methylated spirit, and in this country and in Germany as denatured alcohol (see p. 730); it is not subject to excise tax.

Tar and its Derivatives.—Like wood vinegar, tar is a complex mixture containing different resins, oils, hydrocarbons, phenols, etc., and yields valuable medicinal products. Official tar is derived from pine wood, and is recognized in the Pharmacopœia as Pix Liquida, or liquid pitch; by distillation it yields the official oil of tar and a hard residue known as black pitch. One of the most important derivatives of wood tar is

Creosote.—This is a mixture of phenol-like bodies consisting chiefly of guaiacol and creosol. Beechwood tar is richer in creosote than that derived from other woods, containing usually about 5 per cent., and is therefore a more economical source. Upon distilling the tar a light and a heavy oily layer are obtained, together with an acid aqueous distillate; the heavy oil is subsequently treated with a concentrated solution of sodium carbonate, to remove acid constituents, and again distilled. That portion of the second distillate heavier than water,

and consisting of impure creosote, is dissolved in a moderately strong solution of potassa or soda; any oily layer separating is removed, and the creosote precipitated by saturating the alkaline solution with sulphuric acid. The alternate treatment with alkali and acid is repeated until the alkaline solution is practically free from color and does not turn brown on heating. The precipitated creosote is finally washed with a weak alkaline solution and water, and distilled, that portion distilling between 200° and 220° C. (392° and 428° F.) being collected.

As wood vinegar contains also small proportions of creosote, the latter may be recovered therefrom by first separating the oily constituents by saturating the liquid with sodium sulphate, treating these with sodium carbonate solution, distilling, and proceeding as above.

When first distilled, creosote is colorless, but gradually assumes a yellowish tint, and, as found in commerce, is rarely free from color; upon exposure to air the color darkens materially. The so-called coal-tar creosote of commerce is unfit for medicinal use and should never be employed when creosote is called for. It consists chiefly of cresols (which see under Coal-tar Products), and unfortunately is sometimes offered as common creosote by unscrupulous dealers. For dispensing purposes only the official wood-tar creosote should be employed, which may readily be distinguished from carbolic acid by its peculiar odor, its lesser solubility in water, its immiscibility with a mixture of glycerin and water, and other tests given in the Pharmacopœia; it does not congeal when cooled to —20° C. (—4° F.), but becomes gelatinous. Creosote is soluble in water to the extent of about 3 drops in a fluidounce, and whenever it is to be dispensed in solution in plain water or lime-water the resulting mixture should invariably be passed through a pledget of cotton, as small particles of insoluble matter sometimes separate, particularly in the case of lime water mixtures.

The name creosote was given to this liquid on account of its power of preserving meat, and is derived from the Greek—κρεας, flesh, and σωζειν, to save, to preserve. Creosote was first separated from wood tar in 1832.

A number of compounds of creosote have been introduced into medicine, of which one is officially recognized in the Pharmacopœia, namely:

Creosote Carbonate.—This compound is designated in the Pharmacopœia as a mixture of the carbonates of various constituents of creosote, chiefly guaiacol and creosol. It is prepared by passing a current of carbonyl chloride, phosgene gas, $COCl_2$, into a fixed alkali solution of creosote; the resulting oily liquid is purified by washing with a weak solution of sodium hydroxide and finally with water.

Creosote carbonate occurs as a clear, colorless or yellowish viscid liquid, insoluble in water but freely soluble in alcohol and soluble in fixed oils. While creosote develops with ferric chloride a violet-blue

color, passing rapidly to grayish-green and brown, creosote carbonate acquires only a yellow color under the same circumstances. Creosote carbonate is sometimes called *creosotal*, and may be dispensed either in capsules or dissolved in some bland oil in form of an emulsion.

Guaiacol. $C_7H_8O_2$ **or** $C_6H_4(OH)(OCH_3)$.—This compound, chemically also known as methyl catechol, is the chief constituent of creosote and upon which the medicinal value of the latter, no doubt, wholly depends. It is contained in creosote to the extent of from 60 to 90 per cent., and is obtained from it by fractional distillation, that portion distilling between 200° and 205° C. (392° and 401° F.) being collected as crude guaiacol; this is treated with ammonia to remove acid compounds and again distilled. The lower boiling fraction is collected, dissolved in ether, and treated with alcoholic solution of potassium hydroxide, which causes the separation of potassium guaiacol, $C_6H_4KOCH_3$, the latter being insoluble in ether. After thorough washing with ether the compound is crystallized from alcohol, decomposed by means of diluted sulphuric acid, and the liberated guaiacol again rectified. Guaiacol is not always found absolutely pure in commerce, the pure article occurring usually in a crystalline state, obtained by dissolving purified guaiacol in petroleum benzin, and then subjecting such a solution to spontaneous evaporation; the addition of a crystal of pure guaiacol facilitates crystallization.

Of late years synthetic guaiacol has been freely offered in crystals. It is made by heating in a tightly closed vessel a mixture of equal molecules of pyrocatechin, potassium hydroxide, and potassium methylsulphate, to a temperature of 170° to 180° C. (338°–356° F.), when the following reaction occurs: $C_6H_4(OH)_2 + KOH + KCH_3SO_4 = C_6H_4OHOCH_3 + K_2SO_4 + H_2O$. The resulting guaiacol may be removed by solution in alcohol or petroleum benzin and purified by recrystallization; or it may be made by heating a solution of metallic sodium, pyrocatechin, and methyl iodide in methyl alcohol; the resulting mixture is freed from methyl alcohol, the residue dissolved in sodium hydroxide solution, filtered, and decomposed by means of hydrochloric acid. The guaiacol thus liberated is distilled and then crystallized at a low temperature.

Guaiacol occurs both in the liquid and crystalline form, the former being the variety usually met with, as the crystals melt readily at 28.5° C. (83.3° F.), and will then remain liquid unless again exposed to a very low temperature. It is soluble in 53 parts of water at 25° C. (77° F.), and is readily soluble in alcohol, glycerin, ether, and acetic acid. When mixed with 10 volumes of sulphuric acid a pure yellowish color is produced, free from a reddish tint; the latter would indicate the presence of creosote. The Pharmacopœia also requires that guaiacol, when shaken with 2 volumes of purified petroleum benzin, shall remain clear and separate on standing into two distinct layers; it shall also form a nearly white mass when heated with 2

volumes of sodium hydroxide solution and then cooled, the mass being soluble in 20 volumes of water; turbidity indicates the presence of oily hydrocarbons.

While the name guaiacol is applied to the monomethyl ether of catechol, the dimethyl ether of catechol, $C_6H_4(OCH_3)_2$, is known as veratrol. It is a colorless, aromatic, oily liquid, having the same boiling point as guaiacol and congealing to a crystalline mass when exposed to cold.

A number of derivatives of guaiacol have been introduced at various times, being chiefly compounds with acid radicals, such as guaiacol camphorate (guaiacamphol), g. carbonate, g. benzoate (benzosol), g. cinnamate (styracol), g. phosphate, g. phosphite, g. salicylate (guaiacol-salol), g. valerate or valerianate (geosote), etc., one of which is officially recognized.

Guaiacol Carbonate. $(C_7H_7O)_2CO_3$ **or** $(C_6H_4OCH_3O)_2.CO$.—This compound, also known as duotal, may be obtained by slowly passing carbonyl chloride, phosgene gas, $COCl_2$, into a solution of guaiacol in sodium hydroxide solution, sodium chloride and guaiacol carbonate being formed; the latter being insoluble is precipitated and washed subsequently with sodium hydroxide solution, after which it is crystallized from alcohol. It occurs as a white crystalline powder, melting between 84° and 87° C. (187.2° and 188.6° F.), and while insoluble in water, it is soluble in chloroform, ether, and alcohol, and to some extent in glycerin and fixed oils.

CHAPTER LIV.

COAL-TAR PRODUCTS AND RELATED COMPOUNDS.

DURING the destructive distillation of coal, itself a modified form of wood, the result of slow decomposition caused by decay and fermentative action, gaseous as well as liquid products are obtained, besides a solid residue known as coke, the process being similar to that occurring in the distillation of wood. The gases are used extensively for illuminating and heating purposes, while the coal tar, which contains benzene, C_6H_6, toluene, C_7H_8, aniline, $C_6H_5NH_2$, naphthalene, $C_{10}H_8$, phenol, C_6H_5OH, cresol, C_7H_7OH, and other important substances, is further distilled, and furnishes, besides a solid residue, known as pitch or asphalt, a light and heavy oil, from which the above compounds are extracted.

The distillate of coal tar, known as light oil, consists chiefly of hydrocarbons having various boiling points, which can be separated from each other by fractional distillation. The most important of these is:

Benzene, C_6H_6, designated by many as benzol, which furnishes a number of valuable derivative products; it is obtained by collecting that portion of light oil distilling between 80° and 90° C. (176° and 194° F.), purifying the same by exposing it to a low temperature, when it crystallizes and is freed from adhering liquid impurities, and redistilling. The U. S. Pharmacopœia recognizes pure benzene among the official reagents and describes it as having a specific gravity of 0.876 at 25° C. (77° F.)$_3$ congealing at 5.2° C. (41.3° F.), and boiling between 79° C. (174.2° F.), and 80.4° C. (176.7° F.). It is insoluble in water, but soluble in 4 parts of alcohol and in ether.

Benzene must not be confounded with benzin, officially known as petroleum benzin, a mixture of hydrocarbons obtained by distillation from American petroleum (which see under Petroleum Products).

Toluene, or Methylbenzene, $C_6H_5CH_3$, is another hydrocarbon of interest to pharmacists as the source of the official benzosulphinide, considered below. It is obtained from the light oil of coal tar by fractional distillation, as a colorless, mobile liquid, resembling benzene, but differing from the latter in boiling between 110° and 112° C. (230° and 233.6° F.), and is not congealing even when cooled to —20° C.(—4° F.). It has a specific gravity of about 0.865 at 25° C. (77° F.).

Naphthalene. $C_{10}H_8$.—This hydrocarbon, frequently also called naphthalin, exists, like benzene and toluene, in coal tar; it is found

in the so-called heavy oil, and is deposited as a dark colored crystalline substance from the fraction collected between 180° and 250° C. (356° and 482° F.). Crude naphthalene is purified by successive treatment with sodium hydroxide and sulphuric acid, to remove acid and basic by-products, after which it is repeatedly heated with concentrated sulphuric acid, being each time distilled with steam, and is finally resublimed. The white naphthalene thus obtained still has a tendency to darken when exposed to air and light, to overcome which it is treated for a short time with a mixture of sulphuric acid and manganese dioxide at waterbath temperature; finally, the product is washed with weak alkaline solution and water and again sublimed.

For pharmaceutical purposes, naphthalene recrystallized from alcohol should alone be used.

Aniline. $C_6H_5NH_2$.—Aniline, also known as amidobenzene and phenylamine, occurs in small quantities in coal tar, but is chiefly manufactured from benzene by adding the latter in small portions to fuming nitric acid, when a dark red liquid is formed, from which, upon addition of water, an oily liquid is precipitated, known as nitrobenzene, $C_6H_5NO_2$. By the action of nascent hydrogen, subsequent mixture with milk of lime, and distillation, nitrobenzene is made to yield a basic fluid, to which the name aniline has been given.

While aniline itself is not used in medicine, it is of interest as furnishing a number of derivatives, both directly and indirectly. It occurs, when freshly distilled, as a colorless, highly refractive, oily liquid, which soon acquires a yellow and finally a brown color when exposed to the air and light. Aniline is capable of forming salts with acids, which are mostly crystallizable.

Diphenylamine, $NH(C_6H_5)_2$, formed by heating aniline hydrochloride with aniline to 240° C. (464° F.), is used as a very delicate reagent for nitric acid, with which it strikes a deep blue color; the official test-solution is made by dissolving 0.1 Gm. of diphenylamine in 50 mils. (or Cc.) of diluted sulphuric acid.

Phenylhydrazine, $C_6H_5NH.NH_2$, is obtained by adding an aqueous solution of sodium nitrite to a solution of aniline in strong hydrochloric acid. To this liquid is added an acid solution of stannous chloride, and the resulting phenylhydrazine hydrochloride is then decomposed with an alkali and the base extracted with ether. It occurs in tabular crystals which melt at 17.5° C. (62.5° F.), and are only slightly soluble in cold water. Phenylhydrazine is used in the manufacture of antipyrine, and hence possesses more or less pharmaceutical interest.

Phenol. C_6H_5OH.—Although the name phenol has been officially adopted for this compound, it will probably continue to be known better by its former official, and still present commercial, name, carbolic acid. One of the reasons for changing the official title was the

fact that a large number of impure products are offered as carbolic acid, and it was deemed wise to designate the official pure article intended for medicinal use by a specific name, universally applied to it by chemists. Chemically phenol is hydroxybenzene, and is the type of a class of compounds which are hydroxyl derivatives of the aromatic hydrocarbons, to which the class name phenols has been given.

Phenol occurs in that portion of the distillate from coal tar which comes over between 100° and 250° C. (212° and 482° F.), in proportions varying from 4 to 10 per cent. Besides the natural product large quantities of phenol are also made synthetically.

Natural phenol may be obtained from the coal tar distillate named above by agitating the same with a 10 per cent. sodium hydroxide solution (a stronger solution is not desirable, since it would dissolve naphthalene and other impurities contained in the oil); upon standing, the mixture separates into two layers, the lower being a solution of sodium phenol, C_6H_5ONa, while the upper consists of the extracted oil. The lower layer is carefully drawn off and treated with hydrochloric or sulphuric acid in such quantity as has been ascertained (by a previous test) to be sufficient for exact decomposition. In some cases the sodium phenol solution, for the purpose of purification, is treated first with about one-eighth of the necessary quantity of acid, whereby homologous phenols are separated, and after the removal of these the solution is decomposed completely by acid. The impure phenol thus liberated rises as an oily layer to the surface, which, after removal, is washed by agitation with concentrated solution of common salt, freed from water by means of calcium chloride, and then distilled between 180° and 190° C. (356° and 374° F.). Upon exposure in cool places the distilled phenol congeals to a crystalline mass, which, after being freed from adhering liquid, is again distilled, that portion coming over below 185° C. (365° F.) being carefully collected and crystallized. Sometimes the phenol before final distillation is treated with potassium dichromate and sulphuric acid. In order to obtain phenol in colorless, loose crystals, it may be recrystallized from boiling petroleum benzin.

While the above method is the one generally followed, some manufacturers extract phenol from a smaller fraction of the coal tar distillate, known as *heavy oil*, and collected between 160° and 220° C. (320° and 428° F.), the treatment being practically identical with that given above.

Synthetic Phenol.—Since 1888 considerable quantities of synthetic phenol have been placed upon the market. This is prepared directly from benzene by first treating it with fuming sulphuric acid and moderately warming the mixture, whereby benzene-sulphonic acid is produced: $C_6H_6 + H_2SO_4 = C_6H_5SO_2OH + H_2O$. The acid thus formed is neutralized with potassium carbonate, yielding potassium benzenesulphonate, and this compound then fused with a large excess of potassium hydroxide, whereby potassium sulphite and potassium

phenol are formed: $2(C_6H_5SO_2OK) + 4KOH = 2H_2O + 2KSO_3 + 2C_6H_5OK$. The potassium phenol finally is treated in solution with hydrochloric acid, in order to liberate the phenol or carbolic acid, which is purified further by distillation: $C_6H_5OK + HCl = C_6H_5OH + KCl$. The advantages of the synthetic method are chiefly the absence of homologous products (cresol, xylene, etc.), as the benzene can be procured of great purity by means of crystallization.

Phenol occurs in crystalline masses and also in the form of loose crystals, having a faint aromatic odor, and should be free from color. It is freely soluble in glycerin and fixed oils; also in alcohol and ether, but requires about 15 parts of water for solution at 25° C. (77° F.). The Pharmacopœia demands that if 10 Gms. of phenol be heated on a waterbath, it shall volatilize without leaving more than 0.05 per cent. of residue. The congealing point of phenol is given as not below 38° C. (100.4° F.), but no mention is made of its boiling point, which should not be higher than 185° C. (365° F.). The German Pharmacopœia gives the congealing point as 39°–41° C. and the boiling point at 178°–182° C., while the British gives the melting point as 39°–40° C., and the boiling point as not higher than 183° C. It must be borne in mind that cresols, which may be present, have a higher boiling point, and that phenol may contain variable proportions of water, which would influence the congealing point, and hence a lower boiling point or a higher melting point will indicate a purer and less hydrated phenol. The vapor of phenol is inflammable.

The Pharmacopœia demands that phenol shall contain not less than 97 per cent. of absolute C_6H_5OH, to be determined volumetrically by precipitation as tribromophenol, $C_6H_2Br_3OH$. The solution used for this purpose is known as Koppeschaar's Solution, and is designated in the Pharmacopœia as tenth-normal bromine solution, although it contains no free bromine; it is a solution of sodium bromate and bromide in such proportions that when treated with hydrochloric acid an amount of bromine is liberated corresponding to 0.007992 Gm. for each mil. (or Cc.) of the solution used, thus constituting it a tenth-normal bromine solution. In the official test an excess of this solution is added to an aqueous solution of phenol together with some hydrochloric acid, and the excess ascertained by addition of potassium iodide and subsequent titration of the liberated iodine by means of sodium thiosulphate solution. Since iodine is liberated by bromine in exact molecular proportions, 1 mil. (or Cc.) of tenth-normal sodium thiosulphate solution corresponding to 1 mil. (or Cc.) of tenth-normal iodine solution, must also correspond in value to 1 mil. (or Cc.) of tenth-normal bromine solution, and the number of mils. (or Cc.) of the sodium thiosulphate solution required in the official assay, when subtracted from the number of mils. (or Cc.) of tenth-normal bromine solution originally added, leaves the number of mils. (or Cc.) of the latter solution necessary for the precipitation, as tribromophenol, of all phenol present.

Four distinct reactions occur during the performance of this test before the data necessary for the calculation of the percentage of phenol present are obtained, namely: 1. The liberation of bromine by means of hydrochloric acid; thus, $NaBrO_3 + 5NaBr + 6HCl = 6NaCl + Br_6 + 3H_2O$. 2. The precipitation of tribromophenol; thus, $C_6H_5OH + Br_6 = C_6H_2Br_3OH + 3HBr$. 3. The liberation of iodine; thus, $2KI + Br_2 = 2KBr + I_2$. 4. The decoloration of the iodine solution; thus, $2(Na_2S_2O_3 + 5H_2O) + I_2 = 2NaI + Na_2S_4O_6 + 10H_2O$. The second equation shows that 94.05 parts of absolute phenol require 479.52 parts of bromine for complete precipitation; hence each mil. (or Cc.) of the bromine solution corresponds to 0.001568 Gm. of C_6H_5OH, for 479.52 : 94.05 : : 0.007992 : 0.001568. The number of mils. (or Cc.) of tenth-normal bromine solution consumed, ascertained as directed above, when multiplied by 0.1568 (0.001568 × 100) and divided by the weight of phenol used for the assay, as represented in the aliquot portion of the solution taken, will express the per cent. of pure C_6H_5OH present in the sample.

Phenol is a powerful poison, and many deaths have been recorded from swallowing the same, either accidentally or with suicidal intent. Oil or glycerin should never be administered after phenol has been swallowed, since both will facilitate absorption of the poison; sodium or magnesium sulphate is considered an efficient antidote, and alcohol, moderately diluted with water, is said to have been used with excellent results in mitigating the caustic effects of phenol on the skin and mucous membranes.

The Pharmacopœia recognizes liquefied phenol under the title Phenol Liquefactum, which is prepared by melting phenol on a water-bath, and then adding for every 9 parts by weight of melted phenol, 1 part by weight of distilled water, and mixing thoroughly. This liquid, if made from official phenol, contains not less than 87 per cent. of absolute C_6H_5OH and 13 per cent. of water. It is miscible with alcohol, ether, and glycerin in all proportions, but on account of the water present will not mix clear with chloroform or olive oil; when diluted with an equal volume of glycerin, it is miscible with water. Liquefied phenol must be kept in a moderately warm room, since it will congeal to a crystalline mass at 13.5° C. (56.3° F.).

Among the many derivatives of phenol, one in particular has in recent years come extensively into use among physicians and in proprietary medicines, and is recognized in our own and several foreign pharmacopœias, namely:

Phenolphthalein. $C_{20}H_{14}O_4$ or $(C_6H_4OH)_2COC_6H_4CO$.—Phenolphthalein, also known as paraphthalein and dihydroxyphthalophenone, is a dibasic derivative of phenol, obtained by heating 10 parts of phenol with 5 parts of phthalic anhydride and 4 parts of sulphuric acid at 120° C. (248° F.) for 10 or 12 hours, when the following reaction takes

place, $2C_6H_5OH + C_8H_4O_3 = C_{20}H_{14}O_4 + H_2O$, the sulphuric acid simply acting as a dehydrating agent to take care of the water formed. The mass is boiled with water to remove the acid, and is then dissolved in dilute sodium hydroxide solution and finally precipitated by means of acetic acid. The precipitate is purified by washing with water, dissolved in absolute alcohol, decolorized with animal charcoal and after filtration is again precipitated by addition of water to the filtrate.

Phenolphthalein occurs as a white or faintly yellowish-white or faintly pinkish-white, odorless, tasteless powder, almost insoluble in water but soluble in alcohol and in ether. Its value as an indicator in volumetric analysis has been long known, and at present it is largely used as a gentle laxative in uncomplicated constipation, given in pill or tablet form, the adult dose being from 1 to 3 grains.

Another phenol derivative recognized in the Pharmacopœia, although but little used in pharmacy, is

Trinitrophenol, also known as *Picric Acid.* $\mathbf{C_6H_2(NO_2)_3OH}$.—This is obtained by first preparing phenolsulphonic acid by action of sulphuric acid on phenol (see page 592), and then adding to this nitric acid in a thin stream and with constant stirring of the mixture as long as nitrous fumes are given off. The reaction $C_6H_5(SO_2OH)OH + 3HNO_3 = C_6H_2(NO_2)_3OH + H_2SO_4 + 2H_2O$ results in the formation of trinitrophenol with elimination of sulphuric acid and water.

Trinitrophenol occurs in pale yellow prisms or scales, soluble in water, alcohol, chloroform, ether and benzene, the solutions staining the skin permanently yellow. While rarely used internally, its aqueous solution is sometimes employed locally, and forms a convenient reagent for the presence of alkaloids.

Cresol. $\mathbf{C_7H_7OH}$ **or** $\mathbf{C_6H_4(CH_3)OH}$.—Under this name the Pharmacopœia recognizes a mixture of three isomeric bodies, which bear the same relation to toluene as phenol bears to benzene, being hydroxyl derivatives of that hydrocarbon. Commercially cresol is obtained from the coal-tar distillate collected between 140° and 220° C. (284° and 428° F.) by treatment with sodium hydroxide solution. By carefully adding to the solution thus produced some water and hydrochloric acid, hydrocarbons, and tarry matter are removed, and the cresols precipitated by adding to the clarified filtrate a further limited quantity of hydrochloric acid, insufficient to liberate the phenol present, which latter remains in solution. The resulting product is redissolved in sodium hydroxide solution and again treated with acid as above, the precipitated liquid being finally fractionated by distillation between 180° and 200° C. (365° and 392° F.). This product is known as crude cresol; it is not recognized in our Pharmacopœia, but is official in Germany. By still further purification and distillation between 190° and 205° C. (383° and 401° F.), the official article is obtained.

Official cresol, also sometimes designated as tricresol, is a colorless or straw-colored refractive liquid, turning yellowish-brown on exposure to light and having a phenol-like odor. It is heavier than water and soluble in about 50 volumes of that liquid, and should form a clear solution with an equal volume of 10 per cent. sodium hydroxide solution. The chief constituents are the three isomers, ortho-, meta- and paracresol, which boil respectively at 185°, 201°, and 198° C. (365°, 393.8° and 388.4° F.). All three possess strong antiseptic, germicidal, and disinfectant properties, and are far less poisonous than phenol.

Cresol is used in pharmacy for the preparation of the official Compound Solution of Cresol, which is made by adding cresol to an equal weight of linseed oil and potash soap, prepared from linseed oil 350 Gms., potassium hydroxide 80 Gms., and water 70 Gms. The mixture is stirred until a clear solution results. Compound solution of cresol is a yellowish-brown to brown saponaceous oily liquid and resembles some of the commercial products known as *creolin*, *lysol*, *sapocresol*, etc.

Crude cresol closely resembles the different grades of crude carbolic acid used for disinfecting purposes; some of the latter are often of very dark, almost black color, and contain considerable tarry matter.

Resorcinol. $C_6H_6O_2$ **or** $C_6H_4(OH)_2$.—Resorcinol, also known as resorcin, was first obtained by fusion of certain resins, such as those of ammoniac, galbanum, guaiac, etc., with potassium hydroxide, but is now made almost altogether from benzene by heating the latter with fuming sulphuric acid to 257° C. (494° F.), whereby benzene-metadisulphonic acid, $C_6H_4(HSO_3)_2$, is produced. This acid is neutralized with milk of lime and decomposed with sodium carbonate, and the solution of sodium benzene metadisulphonate thus obtained evaporated to dryness; the residue fused for several hours with sodium hydroxide yields sodium resorcin and sodium sulphite. Boiling an aqueous solution of the saline mass expels sulphurous acid, and, upon extracting the tar-like residue with ether and distilling, impure resorcinol is obtained, which is purified by sublimation and recrystallization from water.

Resorcinol is chemically known as metadihydroxybenzene, which shows it to be a diatomic phenol, $C_6H_4(OH)_2$; two isomerides are also known, namely, ortho- and paradioxybenzene, designated as catechol or pyrocatechin and hydroquinol or hydroquinone, respectively.

The Pharmacopœia requires that resorcinol shall contain not less than 99.5 per cent. of pure metadihydroxybenzene, which is determined in a manner almost identical with that prescribed for the assay of phenol on page 706, each mil. (or Cc.) of tenth-normal bromine solution consumed corresponding to 0.001834 Gm. of pure resorcinol. Three molecules of bromine react with 1 molecule of resorcinol to form 1 molecule of tribromoresorcinol and 3 molecules of hydrobromic acid, and as in the case of the phenol assay, the excess of bromine liberated in the official assay by the hydrochloric acid sets free an equivalent

amount of iodine from the potassium iodide, which is then titrated with sodium thiosulphate solution.

Pure resorcinol occurs in colorless crystals, which readily assume a pink tint, and finally turn red upon exposure to air and light; it must, therefore, be carefully preserved, in tightly stoppered bottles, in a dark place. Solutions of resorcinol also become rapidly colored, hence should always be dispensed in dark amber-colored vials.

Acetanilid. C_8H_9NO **or** $C_6H_5NHC_2H_3O$.—This compound, also known as phenylacetamide, is made direct from aniline, and hence is indirectly a benzene derivative. Chemically it is the monoacetyl derivative of aniline. It is one of a class of chemical compounds known as anilides, which are derived from aniline by replacement of one or both hydrogen atoms of the amido group NH_2, by alcohol or acid radicals, hence both alcohol and acid anilides are known to chemists. Acetanilid is prepared by heating in a flask connected with a reflux condenser a mixture of equal parts of aniline and glacial acetic acid until a small portion of the mixture removed from the flask congeals on cooling; the mass is then distilled, when water and acetic acid first pass over, and afterwards acetanilid, which is subsequently recrystallized from boiling water. The reaction involved in this process consists in the formation of aniline acetate, which upon heating is split up into acetanilid and water, as shown by the equations $C_6H_5NH_2 + HC_2H_3O_2 = C_6H_5NH_2HC_2H_3O_2$ and $C_6H_5NH_2HC_2H_3O_2 = C_6H_5NHC_2H_3O + H_2O$.

The name antifebrin has also been given to acetanilid and is officially recognized as a synonym in the Pharmacopœia. A compound closely allied to acetanilid is commercially known as *exalgine;* it is methylacetanilid, $C_6H_5NCH_3C_2H_3O$, and differs from acetanilid in having both hydrogen atoms of the amido group replaced, one by an alcohol radical and the other by an acid radical.

Acetphenetidin. $C_{16}H_{13}NO_2$ **or** $C_6H_4(OC_2H_5)NH.CH_3CO$.—The true chemical name for this compound is acetparaphenetidin, which is recognized in the French and Austrian Pharmacopœias by the same name as in our own, but is called phenacetin in the British, German, and Swiss Pharmacopœias. Chemically it is the monoacetyl derivative of paramidophenetol and is indirectly a benzene derivative, being made from phenol by first acting on the same with diluted nitric acid, whereby ortho- and paranitrophenol, $C_6H_4(NO_2)OH$, are formed. These are separated by distillation with steam, the residuary para-compound being afterward decolorized and crystallized and treated with sodium hydroxide, forming sodium nitrophenol, $C_6H_4(NO_2)ONa$. By heating this compound with ethyl iodide, paranitrophenetol, $C_6H_4NO_2OC_2H_5$, and sodium iodide are obtained; the former being converted into para-amidophenetol or paraphenetidin, $C_6H_4NH_2OC_2H_5$, by the action of nascent hydrogen obtained from zinc and hydro-

chloric acid. If paraphenetidin be then boiled for some time with glacial acetic acid it is converted into acetparaphenetidin, just as acetanilid is formed from aniline.

Acetphenetidin is sparingly soluble in water, about 1 Gm. in 1310 mils. (or Cc.) at 25° C. (77° F.), but is readily soluble in alcohol. It may be adulterated with acetanilid, for which the Pharmacopœia gives the following simple test, easily applied at the dispensing counter: If 0.1 Gm. of acetphenetidin be boiled with 10 mils. (or Cc.) of water it should yield a solution, which when cooled and filtered, should not become turbid upon the addition of bromine test-solution drop by drop, with agitation, until the solution remains permanently yellow.

Antipyrine. $C_{11}H_{12}N_2O$ or $C_3HN_2O(CH_3)_2.C_6H_5$ or $C_6H_5N.CO.CH:C.(CH_3).N(CH_3)$.—Antipyrine is one of the oldest synthetic antipyretics, having first been made by Knorr in 1873. It is usually prepared by heating phenylhydrazine, $C_6H_5HN.NH_2$, with acetoacetic ether, $CH_3CO.CH_2CO.OC_2H_5$, whereby phenylmethylisopyrazolon, $C_6H_5N.CO.CH : C(CH_3).NH$, is produced. This compound is then dissolved in methyl alcohol and treated with methyl iodide, the latter uniting and forming an addition compound, which, when further treated with sodium hydroxide solution, separates antipyrine in the form of a heavy oil, hydriodic acid being split off. The oily product is then dissolved in ether or toluene and crystallized. Antipyrine may also be made by heating methylphenylhydrazine with acetoacetic ether, alcohol and water being split off, thus, $C_6H_5HN.NHCH_3 + CH_3CO.CH_2CO.OC_2H_5 = C_6H_5N.CO.CH : C(CH_3)N(CH_3) + C_2H_5OH + H_2O$.

The true chemical name for antipyrine is *phenyldimethylpyrazolon*, and it has also been known by such names as *anodynine*, parodyne, and *methozine*. The official name of antipyrine in the British Pharmacopœia is *Phenazone*, and in the French Pharmacopœia, *Analgésine*. In Germany it is usually prescribed by the official Latin title (*Pyrazolonum Phenyldimethylicum*) of that Pharmacopœia.

Antipyrine is a well characterized base and forms salts with acids by direct addition. It is soluble in less than its own weight of water and in its own weight of alcohol or chloroform. An admixture of acetanilid may be readily detected by the disagreeable odor of phenyl isocyanide developed if a warm solution of the suspected substance in sodium hydroxide solution be mixed with some chloroform and again warmed.

Many chemicals have been found to be incompatible with antipyrine, thus sodium bicarbonate and salicylate, in solid form, hydrated chloral and butyl chloral, ferrous sulphate, hydrocyanic acid, phenol, and mercurous and mercuric chlorides. Nitrites in neutral or alkaline solution do not affect antipyrine, but in acid solution, when nitrous

acid is liberated, yield a deep green-colored liquid, due to the formation of isonitroso-antipyrine.

A number of salts of antipyrine have been introduced, some under specially coined fancy names, such as *salipyrine* for antipyrine salicylate, *benzopyrine* for antipyrine benzoate, *tussol* for antipyrine mandelate, etc.

Betanaphthol. $C_{10}H_7OH$.—This compound, formerly known as naphthol and still recognized under that name in the British and German Pharmacopœias, occurs naturally in coal tar, but is usually made artificially from naphthalene, to which it bears the same relation as phenol bears to benzene. Naphthalene, when heated with concentrated sulphuric acid, forms naphthalenesulphonic acid, $HSO_3C_{10}H_7$, of which two varieties occur, designated as alpha- and betanaphthalenesulphonic acid; the formation of these two acids depends upon the temperature employed, the alpha acid being produced at water-bath temperature, and even below, and is changed to the beta variety as the temperature is raised beyond this point. Both acids, when treated with milk of lime, yield the respective calcium naphthalenesulphonates, from which the corresponding sodium salts are obtained by decomposition with sodium carbonate. The sodium salts fused with caustic soda yield sodium naphthol and sodium sulphite, which, by treatment with hydrochloric acid, are converted into sodium chloride and alpha- or betanaphthol, as the case may be. The final product is further purified by sublimation and recrystallization from water.

The Pharmacopœia recognizes only betanaphthol, and, as alpha-naphthol is more poisonous than the official variety, the formation of betanaphthalenesulphonic acid only is sought to be insured by heating the mixture of naphthalene and sulphuric acid to 200° C. (392° F.).

Commercial betanaphthol is sometimes contaminated with alpha-naphthol, which latter may be detected by the violet color produced if to a cold saturated aqueous solution be added a few drops of iodine test-solution followed by an excess of sodium hydroxide test-solution.

Betanaphthol furnishes a number of derivative products which have been introduced into medicine, such as *benzonaphthol* or naphthol benzoate—*betol* or naphthol salicylate, known also as naphthalol, naphthosalol or salinaphthol—*hydronaphthol—asaprol* or calcium naphtholsulphonate—*alumnol* or aluminum naphtholsulphonate, etc. (An account of these products and their properties can be found in the *National Standard Dispensary*, 1916, p. 321.)

Benzosulphinide. $C_7H_5NSO_3$ **or** $C_6H_4SO_2.CONH$.—This compound also known as Glusidum and still better as Saccharin, is chemically the anhydride of orthosulphamidebenzoic acid. When toluene is treated

with sulphuric acid at 100° C. (212° F.) a mixture of ortho- and paratoluenesulphonic acids, $C_6H_4(CH_3)SO_3H$, is formed, from which the respective calcium salts may be obtained, and then by mutual decomposition with sodium carbonate, the corresponding sodium salts. From these a mixture of ortho- and paratoluenesulphochlorides, $C_6H_4(CH_3)SO_3Cl$, is obtained by the action of phosphorus pentachloride and the paramodification caused to crystallize by strong cooling. If dry ammonia gas be allowed to act on orthotoluenesulphochloride, the corresponding sulphamide, $C_6H_4(CH_3)SO_2NH_2$, is formed, which upon oxidation with potassium permanganate yields potassium orthosulphamidebenzoate. The latter salt when decomposed by means of an acid does not yield free orthosulphamidebenzoic acid, but instead the acid splits up into its anhydride and water, the former of which may then be crystallized from alcohol or boiling water.

Benzosulphinide is not very soluble in water, requiring about 290 parts at 25° C. (77° F.), but is soluble in 25 parts of boiling water or in alcohol. Although it has been suggested as a desirable sweetening agent for food in certain diseases, it hardly seems to merit a place in the Pharmacopœia and is not used in any of the official preparations. It is said to have 500 times the sweetening power of sugar and its sweet taste is perceptible even in dilutions of 1 to 10,000. Since parasulphamidebenzoic acid does not possess a sweet taste, its presence would materially reduce the sweetening power of the official article; the British Pharmacopœia recommends a special test for the same by allowing a strong solution to crystallize and then testing the melting point of the crystals. Crystals of parasulphamidebenzoic acid melt at 280° to 283° C. (536°–541.4° F.), while those of benzosulphinide melt between 219° and 222° C. (426.2° and 431.6° F.).

The solubility of benzosulphinide in water is greatly increased by the presence of alkali carbonates and bicarbonates, orthosulphamidebenzoates being formed. The sodium salt, $C_6H_4COSO_2N.Na + 2H_2O$ (see p. 584), is commercially known as *soluble saccharin*, *soluble gluside*, and *crystallose*, and should not be confounded with the official benzosulphinide, which is sometimes designated as insoluble saccharin.

Besides the name saccharin, the following have also been applied to commercial benzosulphinide: *neosaccharin*, *glucusimide*, *benzoylsulphonimide*, etc.

Methylthionine Chloride. $C_{16}H_{18}N_3ClS + 3H_2O$.—The full chemical name of this compound is tetramethylthionine chloride, but it is better known by its trade name, methylene blue, which has also been adopted as one of the official synonyms. It may be prepared by treating a solution of amidodimethylaniline, known also as dimethyldiamidobenzene, $C_6H_4(NH_2)N(CH_3)_2$, in hydrochloric acid with hydrogen sulphide and then with ferric chloride. It occurs both as a dark green crystalline powder and in form of prismatic crystals having a bronze like luster, which dissolve readily in water with deep blue color. The

Pharmacopœia requires that upon incineration of the salt not more than 1 per cent. of ash shall remain, which must be free from zinc.

Methylene blue is usually dispensed in capsules, either dry or in form of a mass. Some little care is necessary to avoid soiling the hands and clothing of the operator. When it is ordered in powder form, the best plan would seem to be to rub the methylene blue into powder, not too fine, in a glass mortar, and divide the powder into the prescribed number of doses on glazed paper, and then carefully transfer to the capsules. If a mass is to be made, methylene blue may be rubbed into powder with half its weight of powdered licorice root and then massed with glucose or some similar excipient. By keeping the hands and pill tile well dusted with licorice powder, it is possible to prevent coloring while the mass is divided into the required number of rod-shaped pieces, which may then be transferred to the capsules in the usual manner with the aid of a long needle.

Commercially, methylene blue is sometimes found as the double chloride of zinc and tetramethylthionine, in which form it is used as a dye, but is unfit for medicinal purposes, hence the test for absence of zinc, mentioned above. It must not be confounded with methyl blue, which is made by treating pararosaniline with aniline and the resulting product with sulphuric acid. A solution of methyl blue, upon the addition of sodium hydroxide, changes to reddish-brown, whereas the color of methylene blue solution changes to violet.

CHAPTER LV.

STARCHES, GUMS, AND SUGARS.

BESIDES cellulose, certain other principles are widely diffused in the vegetable kingdom, which are of more or less interest to pharmacists, either as useful medicinal agents or because they must be excluded in the preparation of certain galenicals. These are known as amylaceous, mucilaginous, and saccharine principles, and are usually designated as starches, gums, and sugars. The investigations of E. Fisher and others regarding the chemical character of these well known plant products have so completely changed the views formerly entertained, and so enriched the knowledge regarding their intimate relationship, that chemists now consider starch, gum, and sugar, and also cellulose, as members of a group designated as saccharides; in regard to their chemical character, they are looked upon as aldehydes ketones, and ether-like anhydrides derived from certain hexatomic alcohols.

Starch.—This substance occurs chiefly in the seeds, roots, and rhizomes of plants, where it appears deposited for the purpose of future nourishment either of the germinating embryo or during the next year's growth of the plant itself. When viewed with the naked eye, starch appears as a structureless substance in the form of a powder, but under the microscope it is seen to consist of round, ovate, lenticular, or polyhedral granules or cells, differing in size and shape according to the source whence the starch has been taken, as may be seen in Fig. 329. Starch granules appear to consist of concentric layers of varying density, arranged around a nucleus or hilum situated in the center of the granule, or more generally at one end or near the margin. The formation of starchy matter and the manner of its deposit belong more properly to the study of physiological botany.

While a valuable dietetic and article of food, starch possesses little or no medicinal virtue, and, as its presence largely interferes with the stability of pharmaceutical preparations, it is sought to be excluded by the use of appropriate menstrua. Starch is insoluble in cold water, strong or diluted alcohol, and ether, but when treated with boiling water solution takes place, and a more or less gelatinous mucilage results upon cooling. This peculiar behavior with water is due to the fact that the starch granules have a very hard outer coating (by some authorities looked upon as a distinct membrane), to which the name farinose or amylin has been given; this is ruptured by the boiling water, after which the white contents of the granule, known as granu-

lose or amidin, are dissolved. Prolonged trituration of starch with sand causes a similar rupture of the farinose, when a portion of the amidin will also be taken up by cold water. Complete solution of the granules does not occur even with boiling water, as the farinose remains undissolved, but it can be rendered soluble by the action of sulphuric acid. If starch paste, made by mixing starch with water heated to 75° C. (158° F.), be boiled for some time, it is gradually

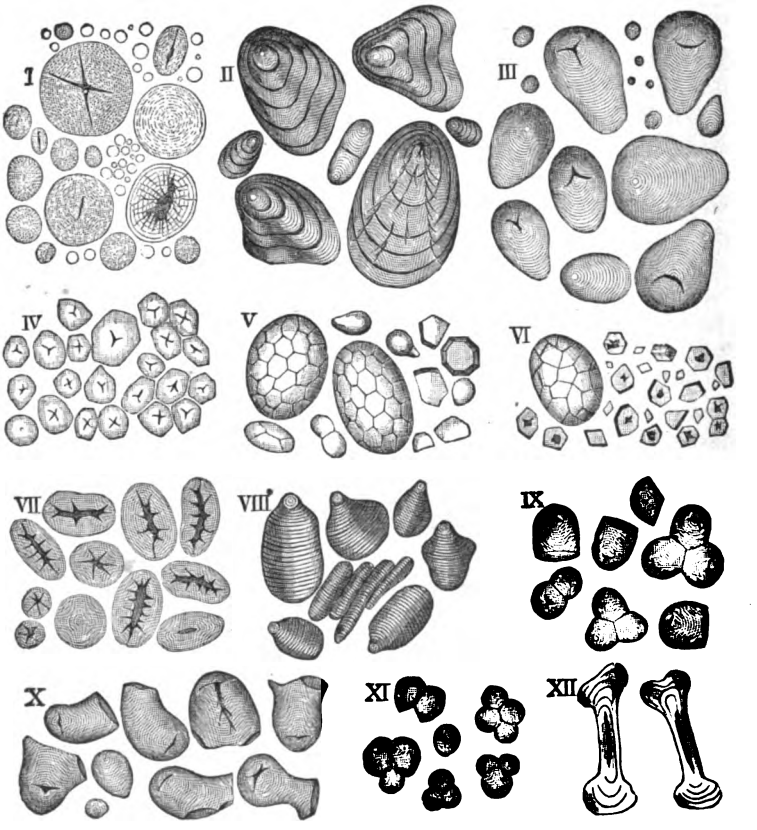


FIG. 332.—I, Wheat starch. II, Potato starch. III, Arrowroot or Maranta starch. IV, Corn starch. V, Oat starch. VI, Rice starch. VII, Bean starch. VIII, Curcuma starch. IX, Tapioca starch. X, Sago starch. XI, Sarsaparilla starch. XII, Euphorbia starch.

converted into a clear liquid capable of being filtered, and if this liquid be added to a large volume of alcohol, a water-soluble modification, known as amylogen, is precipitated in the form of a white powder; this amylogen may be preserved under alcohol, and as long as it is not dried will remain soluble in cold water. Amylogen is likewise produced if starch be mixed with 16 or 18 times its weight of glycerin and then kept at a temperature of 190° C. (374° F.) for about a half-hour, the resulting clear liquid being then precipitated as above stated. Satu-

rated solutions of calcium chloride and potassium iodide effect the same change without the aid of heat.

In composition starch is isomeric with cellulose, but differs from it in physical and many chemical properties. The most delicate reagent for starch is iodine, which strikes a characteristic blue color with cold solutions of starch, and in the form of solution is used to detect starch in vegetable tissues. Conversely, starch mucilage is extensively employed in iodimetry as an indicator; the union between starch and iodine, is, however, a very feeble one, and not considered to be of a chemical character, as it is easily broken up by heat.

All air-dried starch when heated at 100° C. (212° F.) to constant weight loses about 14 per cent. of water, which is gradually reabsorbed on exposure to the air; if anhydrous starch be mixed with a small quantity of water, it absorbs the same with evolution of heat, as certain inorganic salts absorb water of crystallization. When heated for some time to 170°–200° C. (338°–392° F.) starch is gradually converted into dextrin and becomes soluble in cold water, losing at the same time its property of being colored blue by iodine. The same result occurs if starch be heated with diluted nitric or sulphuric acid, the change, however, taking place in less time and at a lower temperature; if the action of the diluted acids be allowed to continue for a longer period, the dextrin is finally converted into dextrose. Diastase, the active ferment of malt, also effects the hydrolysis of starch into dextrin, and finally into a kind of sugar, differing, however, from dextrose and known as maltose; for this reason starch paste is used in the valuation of malt extracts. The value of proper mastication of bread and other starchy food depends upon a thorough admixture with saliva, which contains a ferment, known as ptyalin, having the same effect on starch as diastase.

Dextrin is extensively made for the market from potato starch, either by the dry heat process above mentioned or by mixing the starch into a paste with water acidulated with nitric acid, pressing the paste into cakes, drying, powdering, and heating for one or two hours at 110° C. (230° F.). Dextrin occurs in two varieties, white and yellow, which are soluble in cold as well as hot water, forming a mucilaginous liquid; it has a sweetish taste, peculiar odor, and is known also as British gum. Iodine colors dextrin pink or reddish, unless unaltered starch is present, when a purplish tint results.

Two substances, allied to starch and isomeric with it in composition are met with in certain drugs; these are lichenin and inulin, the former occurring in cetraria and the latter in inula, taraxacum, etc. *Lichenin*, known also as moss starch, is obtainable from Iceland moss and other lichens; it is soluble in boiling water and gelatinizes upon cooling; iodine imparts to it a yellow or brown color. *Inulin*, found in place of starch in the roots and underground stems of many Compositæ, forms a clear solution with boiling water and does not gelatinize upon cooling; continued boiling with water converts it into sugar,

known as fructose. It is colored yellow by iodine and does not occur in the form of concentric layers, nor does it contain a definite and constant proportion of water like starch.

Starch is obtained for use by washing it out with water from the material containing it, the mixture being transferred to large sieves or straining bags, which allow the starch to pass through with the water and retain the cellular fiber. In the case of potatoes, these are first grated, while wheat, corn, etc., are treated in the form of flour. Since cereals contain a nitrogenized principle or ferment, called gluten, intimately mixed with the starch, this is removed either by means of incipient fermentation not affecting the starch, or it may be separated by kneading the flour in muslin bags while a stream of water continually falling on it washes out the starch, leaving the gluten behind. The different varieties of starch can best be distinguished from each other by their shape and size under the microscope, but some show also differences in their behavior with hot water and also hydrochloric acid.

Official starch, recognized in the Pharmacopœia by the general Latin term *amylum*, is corn starch, and is used in preparing the official glycerite of starch. Starch was known to the ancients, who applied the name amylum (derived from the Greek μύλος a millstone, and the prefix ἀ, meaning privative or without) to the substance, because starch could be obtained without grinding between stones, as in the case of flour.

Gums.—These are amorphous translucent substances, in all probability excretory products, obtained usually as exudations. They differ from starch in being wholly or partly soluble in cold water and in not being colored blue by iodine; the blue coloration produced in tragacanth is due solely to the presence of starch. Gums may be divided into two classes, which differ from each other in physical as well as chemical properties; for convenience they are known as gums and mucilages, respectively. As stated on page 376, gums are precipitated from their aqueous solution by strong alcohol, spirit of nitrous ether and solution of ferric chloride, the precipitate in the last case being of a gelatinous character. Diluted alcohol, containing less than 60 per cent. by volume of absolute alcohol, is capable of dissolving gums (the quantity taken up increasing with the decreasing proportion of alcohol present), but glycerin has no solvent effect whatever, although it mixes clear with aqueous solutions of gums. The most delicate reagent for true gum is solution of lead subacetate, which still causes slight opalescence in solutions containing 1 part of acacia in 10,000 parts of water.

True gums consist largely of arabin or arabic acid combined chiefly with calcium, together with potassium and magnesium. Mucilages consist partly of soluble and partly of insoluble principles, and in some cases contain also starch. Acacia and tragacanth are the official representatives of the two classes in the Pharmacopœia, but the muci-

lages are met with also in althæa, elm bark, linseed, sassafras pith, etc. The soluble portion of tragacanth is not precipitated by alcohol or solution of lead subacetate, like arabin, and the insoluble portion is often tinged blue by iodine, as stated above. The so-called gum exuding from cherry, peach, and plum trees must also be classed with the mucilages.

Arabin, or arabic acid, to which when properly dried at 100° C. (212° F.) the empirical formula $2C_6H_{10}O_5 + H_2O$ or $C_{12}H_{22}O_{11}$ has been assigned, may be obtained from mucilage of acacia, after acidulation with hydrochloric acid, by precipitation with alcohol as a milk-white mass of acid reaction and liberating carbon dioxide from carbonates. When dried, it absorbs water and swells, but does not dissolve until lime-water has been added.

Metarabic acid, metarabin or cerasin, occurs in the insoluble portion of cherry gum, and may be obtained from acacia by heating the same for some time at 120°–150° C. (248°–302° F.), when the latter loses its solubility in water, but absorbs the latter and swells. If the acacia thus treated be acidulated with hydrochloric acid and alcohol added as above, a substance is obtained which is likewise insoluble in water, but is soluble in lime-water, soda solution, and similar alkaline liquids, being restored to arabin.

Parabin, which is isomeric with arabin, is found in agar-agar or Ceylon moss; it is without acid reaction, swells to a jelly with water, and is dissolved by dilute mineral acids, but precipitated by alkalies and alcohol.

Under the name Agar, the Pharmacopœia recognizes the dried mucilaginous substance extracted from certain marine algæ found on the eastern coast of Asia. It is insoluble in cold water, but slowly soluble in boiling water; a 1 per cent. solution made by boiling agar with water for 10 minutes yields a stiff jelly on cooling. A one-tenth per cent. aqueous solution of agar, when cooled does not yield a precipitate with tannic acid, which distinguishes agar from gelatin, and is not colored blue upon addition of iodine solution, showing the absence of starch.

While chiefly used as a culture medium in bacteriology, in the form of agar jelly, agar is also prescribed for internal administration in doses of 10 Gms., or 2½ drams, as a laxative.

Traganthin and bassorin are names given to the pectin-like principle present in tragacanth and allied products to the extent of 60 or 70 per cent. It is insoluble in cold and hot water, but absorbs the same, swelling to a gelatinoid mass, and is soluble in alkaline liquids. Besides bassorin, the mucilages contain also 8–10 per cent. of water-soluble principles, and in some cases unaltered starch.

Carragheen is the mucilaginous constituent of Irish moss, or chondrus. It is not precipitated by alcohol, and on treatment with diluted sulphuric acid yields a kind of sugar known as galactose.

When treated with boiling nitric acid gums are converted into

mucic, saccharic, and oxalic acids. By continuous boiling with water acidulated with sulphuric acid some gums yield arabinose and others galactose, products closely allied to the sugars; of these, galactose is capable of fermentation, while arabinose is unfermentable.

The name gum is derived from the Greek *κομμι*, and this from the Egyptian kami, applied to acacia, which was used nearly four thousand years ago as an adhesive agent in painting.

Very closely allied to the gums are the pectous substances, a class of non-nitrogenous bodies widely distributed in plants and without definite character. Unripe acidulous fruits and certain succulent roots contain a peculiar body, called pectose, which, under the influence of a ferment known as pectase in connection with light and heat, and, in the case of fruits, of organic acids also, is changed into pectin, and finally into pectosic acid or vegetable jelly, to which is due the gelatinization of certain fruit juices as well as the infusions of gentian, taraxacum, senega, and other roots. The alkali salts of pectosis acid being soluble, advantage is frequently taken of this in pharmaceutical preparations to prevent gelatinization; as, for instance, the use of ammonia water in fluidextract of senega.

Unripe green fruits owe their hardness to the presence of pectose, and become softer as the latter is gradually changed to pectin during the ripening process.

The name pectin is derived from the Greek *πηκτός*, meaning curdled.

Sugars.—Although for pharmacuetical purposes but three kinds of sugar are employed, chemists include under the general term of sugars a much larger class of compounds, belonging to the carbohydrates and characterized by a more or less sweet taste. For convenience, sugars are divided into two main groups, known as monosaccharides and disaccharides. The name polysaccharides is applied to a third group of carbohydrates, such as starches, gums, cellulose, etc., which have no sweet taste, but yield simple sugars after repeated cleavage induced by boiling with dilute acids and other methods.

Monosaccharides comprise those sugars which cannot be broken up into two or more sugars of simpler character, and are looked upon as aldehydes and ketones derived from such alcohols as erythritol ($C_4H_6(OH)_4$), arabitol and xylitol ($C_5H_7(OH)_5$), mannitol and dulcitol ($C_6H_8(OH)_6$), and others. These sugars do not all contain the same number of carbon atoms, and for convenience are divided into *hexoses*, $C_6H_{12}O_6$, dextrose, fructose, and galactose; *pentoses*, $C_5H_{10}O_5$, arabinose and xylose (wood sugar); *tetroses*, $C_4H_8O_4$, erythrose; and so on according to their carbon content, some being known in which nine carbon atoms are present. Only the hexoses are of special interest to pharmacists, and to these the group name *glucoses* is often applied.

As a rule, they crystallize imperfectly or with difficulty, and with few exceptions are directly fermentable.

Dextrose. $C_6H_{12}O_6$.—This, the best known member of the group of hexoses, occurs in commerce in the fluid, semifluid, and solid form; the two former are usually designated as glucose, and the latter as grape sugar or starch sugar. In nature dextrose is found associated with fructose or fruit sugar in numerous fruits and in honey; it occurs also in certain secretions of the human body as the result of a disease known as diabetes mellitus. Artificially, it is manufactured on a large scale from corn starch by treatment with diluted sulphuric acid, the process being conducted in both open and closed converters, of which the latter require the application of a higher heat, but a shorter time, to complete the change. As stated on page 717, the first action of the diluted acid is to change the starch into dextrin, which is finally converted into dextrose; liquid or syrupy glucose usually contains unconverted dextrin, while in the solid grape sugar the complete conversion into dextrose has been carried out. Corn starch is always mixed with gluten, which is removed by treatment with sodium hydroxide, after which the starch is mixed with water to a creamy consistence and run into the diluted acid and heated by means of steam until all starch has been converted; the acid is then neutralized by means of calcium carbonate and the liquid filtered, passed through animal charcoal, and concentrated. The name Corn Syrup has been applied to a liquid glucose occurring as a colorless or light yellowish sweetish syrup of 1.40–1.43 specific gravity and containing from 40 to 60 per cent. of dextrose and from 30 to 40 per cent. of dextrin.

The Pharmacopœia recognizes glucose as a syrupy product consisting chiefly of dextrose and dextrins. Official glucose, also known as Syrupy Glucose and Liquid Glucose, should not contain more than 21 per cent. of water and, upon ignition, should yield not more than 1 per cent. of ash. The limit of free acid has been fixed at not more than 0.059 Gm. (calculated as sulphuric acid) for 100 Gms. of glucose.

Grape sugar separates as a granular crystalline deposit in honey, and can be obtained in a hydrated form, $C_6H_{12}O_6 + H_2O$, in small, wart-like crystals from its aqueous or hydro-alcoholic solution; from a hot solution in alcohol or methyl alcohol it separates in anhydrous prismatic crystals. It is soluble in very nearly its own weight of water and in 50 parts of alcohol at 15° C. (59° F.), the solutions possessing a far less sweet taste than those of ordinary sugar. At 60° C. (140° F.) grape sugar softens, and at 86° C. (186.8° F.) melts completely.

Dextrose is directly fermentable, its solutions are not affected by strong sulphuric acid, but when heated with alkali hydroxides acquire a dark color; upon addition of ammoniacal solution of lead acetate dextrose is precipitated from its solution, but is not affected by neutral or basic lead acetate.

Various tests can be used for the detection of dextrose, such as Trommer's test (cupric sulphate, solution of potassium hydroxide, and heat), causing a deposit of brick-red cuprous oxide; Moore's test (solution of potassium hydroxide and heat), causing a dark, almost black, color; Boettger's test (bismuth subnitrate, solution of potassium hydroxide and heat), causing a black precipitate of metallic bismuth, and others. For the quantitative determination of dextrose volumetric alkaline solution of cupric tartrate, known as Fehling's Solution, is usually employed; each mil. (or Cc.) of this solution corresponds to 0.005 Gm. of anhydrous dextrose. When Fehling's Solution is boiled in the presence of dextrose, yellowish hydrated cuprous oxide is first formed, which is finally changed into the anhydrous brick-red variety. Since dextrin also reduces the cupric salt of Fehling's Solution, its absence must first be ascertained in all quantitative determinations by this method. Barfoed's Solution, consisting of 13.3 Gms. of crystallized cupric acetate and 2 Gms. of glacial acetic acid in 200 mils. (or Cc.) of water, suffers reduction with all glucoses, but not with dextrin.

The name dextrose was given to this particular sugar on account of its dextro-rotatory power, since it invariably deflects the ray of polarized light to the right when examined by means of a polariscope. An explanation of the uses of the polariscope can be found on pages 602 and 603 of the Pharmacopœia.

The British Pharmacopœia recognizes an official syrup of glucose, made by mixing commercial liquid glucose with twice its weight of syrup.

Fructose, or **levulose,** is of interest chiefly as a natural constituent of honey; it occurs also associated with dextrose in many fruits, and is therefore known as fruit sugar. The name levulose was given it because it is lævo-rotatory—that is, causes the plane of polarized light to deviate to the left. When pure, it occurs as a colorless or faintly yellowish syrup of very sweet taste, which crystallizes with great difficulty; it remains in the liquid portion of honey after all the granular dextrose has been removed. As stated under Starch fructose is formed also by prolonged boiling of inulin with diluted acids. The term inverted sugar is usually applied to the mixture of dextrose and fructose, whether obtained by inversion of cane sugar by means of diluted acids and heat, or by some special ferment, such as that supplied by bees in the manufacture of honey.

Natural honey contains from 65 to 80 per cent. of a mixture of dextrose and levulose, together with small portions of cane sugar, besides 20 or 30 per cent. of water and about 0.1 per cent. of formic acid. During the clarification of honey the acid is generally dissipated, and possibly on this account clarified honey is more prone to fermentation than the crude article. Commercial honey is frequently adulterated with a solution of glucose and dextrin; the latter can be detected by addition of an excess of official alcohol to an aqueous solution of

honey. Any dextrin present will be precipitated in the form of white flocculi.

Disaccharides appear to be the result of condensation of two or more molecules of one or any two members of the group of glucoses, water being eliminated at the same time; hence they may be considered as ether-like anhydrides; thus, $2C_6H_{12}O_6 = C_{12}H_{22}O_{11} + H_2O$. In support of this view, the members of this group have been found to take up water and split up into equal molecules of glucoses if heated with diluted acids. These sugars are darkened by strong sulphuric acid, and form colorless combinations with the alkalies, differing in these respects from the glucoses. The more important members of the group are sucrose or cane sugar, lactose or milk sugar, and maltose or malt sugar; mycose, identical with trehalose, is of some interest as occurring in ergot. With the exception of malt sugar, the members of the cane sugar group can be fermented only after previous conversion into one of the glucoses.

Sucrose, $C_{12}H_{22}O_{11}$, officially recognized as *Saccharum*, is obtained from sugar cane, sorghum, and the common European sugar beet. While immense quantities of sugar are prepared in this country direct from the juice of the cane, considerable amounts are imported also in the form of raw or crude sugar for refining purposes.

Recently collected sugar cane yields by crushing and expressing about 80 per cent. of juice, which contains from 78 to 84 per cent. of water, 16 to 21 per cent. of sugar, 0.3 to 0.4 per cent. of mucilaginous, resinous, fatty, and albuminous matters, and nearly the same amount of salts. The juice is a grayish, turbid, sweet liquid, which is clarified by heating, a little lime being at the same time added for the purpose of neutralizing free acid; it is then concentrated by rapid evaporation in open pans, transferred to coolers, where it is frequently stirred, and afterward into casks perforated at the bottom and arranged in such a manner that the liquid portion may drain off and be collected in suitable tanks. The granular solid product thus obtained constitutes the *raw* or *muscovado sugar* of commerce; the liquid portion is known as *treacle* or *molasses*. Raw sugar is refined by dissolving it in water, the solution is heated with blood, the impurities are skimmed off, and the liquid is filtered through recently burned granular animal charcoal. The clear and colorless filtrate is concentrated in a vacuum pan, and when of sufficient density run off into conical molds, the narrow orifice of which is closed by a plug. It solidifies as a dense crystalline mass, which is drained by the removal of the plug, and freed from the remaining colored mother-liquor by percolating through it a concentrated solution of pure sugar, after which it is dried and sent into commerce as *refined* or *loaf sugar*. By concentrating the mother-liquors they are made to yield more sugar of an inferior grade, until finally a thick syrupy liquid is obtained, which refuses to crystallize, and is known as *sugar-house molasses*, and in England as treacle.

The method of obtaining sugar from the sugar beet is very similar to that described above, but is attended with greater difficulties, owing to the presence of larger quantities of proteids and of other foreign constituents.

Until 1825 sugar cane was practically the sole supply of sucrose, after which time improved methods were devised for producing sugar from beets on a commercial scale. The presence of sugar in the common forage beet was discovered by Marggraf in 1747, and by scientific cultivation the sugar content has been gradually increased from 6 per cent. to nearly 20 per cent., although the full amount is never obtained. At present the beet sugar industry has grown to enormous proportions, and more than one-half of the world's supply of sugar is today obtained from the sugar beet; large quantities of beet sugar are manufactured in the states of Colorado, Nevada, and Utah.

Hard commercial sugars, dried by artificial heat, contain probably 99 per cent. of sucrose, whereas the softer sugars which have been merely centrifugated may contain from 4 to 5 per cent. of water.

Sucrose is soluble in half its weight of water at 15° C. (59° F.), and in 175 parts of alcohol at the same temperature; it is thus seen to be more soluble in water and less soluble in alcohol than glucose. A saturated solution of cane sugar at 15° C. (59° F.) contains 67.72 per cent. of sugar and has a specific gravity of 1.345; one liter contains 910.8 Gms. of sugar and 434.2 Gms. of water. Official syrup is, therefore, a little less than saturated, containing 64.54 per cent. of sugar. While dextrose melts at 80° C. (176° F.), dry cane sugar remains unaltered at this temperature, but melts at 160° C. (310° F.), congealing afterwards to a slightly colored, glassy mass. Heated to 180° C. (356° F.), cane sugar splits up into dextrose and a product isomeric with starch and dextrin, known as levulosan; above 205° C. (401° F.), a dark brown, thick liquid of complex composition and bitter taste results, to which the name *caramel* has been given.

If cane sugar be heated with diluted (5 per cent.) sulphuric acid, it is changed into *inverted sugar*, a mixture of equal molecules of dextrose and fructose, and is only then capable of fermentation; certain ferments produce the same effect. Sucrose is always dextrorotatory, but becomes less so after inversion, as the fructose then present exercises its lævo-rotatory effect on the plane of light.

The purest sugar obtainable is that known as cut-loaf sugar, which is the best kind for the preparation of syrups and similar solutions, but is not so convenient for use as granulated sugar. The Pharmacopœia demands the absence of more than 0.5 per cent. of invert sugar, to be determined by boiling a solution of 20 Gms. of sugar with Fehling's Solution, collecting the precipitated cuprous oxide on an asbestos filter and, after thorough washing with hot distilled water, alcohol and ether, drying it at 100° C. (212° F.); it should weigh not more than 0.155 Gm.

Cane sugar is used as a valuable preservative for many otherwise

unstable solutions, and its sweet taste renders it a desirable adjuvant in prescriptions. It is also known to increase the solubility of several metallic oxides and vegetable principles.

Lactose. $C_{12}H_{22}O_{11} + H_2O$.—Sugar of milk, which is recognized in the Pharmacopœia by the Latin name *Saccharum Lactis*, is obtained from the milk of mammalia, in which it is found to the extent of from 3 to 6 per cent. It appears to be present in larger proportions in the milk of herbivorous animals than in that of the carnivoræ, and is said to exist also in the fruit of Achras sapota, a tree of the West Indies, this being the only known case of its occurrence in the vegetable kingdom. Milk sugar is obtained by crystallization from the whey or thin fluid remaining after removal of the casein or albuminous principle by coagulation. The crude granular product is purified by resolution, filtration, and recrystallization. Prior to 1890 the world's supply of milk sugar was furnished by Europe, chiefly Switzerland, but since then large quantities are being manufactured in this country, the present annual production being estimated at about 1,500,000 pounds.

The crystals of sugar of milk contain 5 per cent. of water, which is not lost until a temperature of 130° C. (266° F.) is reached. They are very hard, and require about 5 parts of water for solution, at 25° C. (77° F.), the solution being far less dense than one of either dextrose or cane sugar of equal concentration, and far less sweet in taste; almost insoluble in alcohol. As found in the shops, sugar of milk is always in the form of powder, which feels gritty between the teeth. In pharmacy it is used exclusively as a diluent in the preparation of triturations, powdered extracts, etc., for which purpose it is admirably adapted, as it is non-hygroscopic.

Like dextrose, sugar of milk is dextro-rotatory, and also reduces an alkaline solution of cupric tartrate, but does not reduce Barfoed's Solution of cupric acetate (see page 722). Boiled with diluted acids, sugar of milk yields dextrose and galactose; the latter crystallizes in large prisms and yields mucic acid, insoluble in cold water when treated with nitric acid, whereas dextrose yields saccharic acid, which is soluble.

Maltose, or malt sugar, is produced by the action of diastase of malt on starch, either during the germination of the barley or when diastase is mixed with starch and water and kept at a temperature of 70° C. (158° F.). It is directly fermentable, and is of considerable interest in pharmacy on account of the part it plays in the fermentation of grain in the manufacture of alcohol. When hydrolyzed by means of diluted acid or by the action of diastase or yeast, maltose splits up into two molecules of dextrose. Maltose crystallizes with one molecule of water, and is readily soluble in water; although strongly dextro-rotatory, it can be distinguished from dextrose, like milk sugar, by means of Barfoed's Solution.

CHAPTER LVI.

ALCOHOL AND ITS DERIVATIVES.

ALTHOUGH, in chemistry, the term alcohol is used to designate a group of compounds derived from hydrocarbons of the methane or fatty series, by replacement of one or more hydrogen atoms by a corresponding number of hydroxyl groups, which have certain chemical properties in common, it is restricted in pharmacy to one substance, chemically known as ethyl alcohol, and recognized in the Pharmacopœia also by the simple term alcohol. When other alcohols are used in pharmacy they are either designated by specific names, such as glycerin, mannitol, etc., or, by adding a qualifying prefix to the word alcohol, as amyl alcohol, methyl or wood alcohol, etc., to distinguish them from ordinary or ethyl alcohol.

Alcohol is obtained in this country almost exclusively from grain, while in Europe potatoes are extensively employed, by a process known as vinous fermentation. Fermentation is a process of decomposition differing from putrefaction in that the resulting products are, as a rule, valuable, or at least useful, and not accompanied by offensive gases; fermentation is usually applied to the decomposition of substances composed of carbon, hydrogen, and oxygen; while if nitrogen and sulphur are also present the term putrefaction is more aptly used, on account of the putrid or foul odor emitted by such bodies during decomposition. Certain conditions are essential to both processes of decomposition, namely, the presence of air, moisture, heat, and certain agents known as ferments. There are fermentations of various kinds, such as saccharine, vinous, mucic, lactic, butyric, and acetous, depending upon the chemical constitution of the substances undergoing change, some of these being in reality oxidation processes not due to fermentative action.

The first step necessary in the manufacture of alcohol is the saccharine fermentation, known also as the mashing process, which consists in the conversion of starch into sugar by means of diastase. This latter substance is produced during the germination of grain, as in the malting of barley. **Malt** is made by well moistening barley with water and spreading it, about two feet deep, on stone floors, in dark rooms; heat is developed, and partial germination is allowed to go on, during which time *diastase* is produced, the barley assuming a darker color and peculiar odor, while the starch of the grain is converted into dextrin and malt sugar. Diastase is capable of converting 2000 times its weight of starch into maltose. When isolated,

it is a white tasteless solid, soluble in water and weak alcohol, but precipitated by strong alcohol, and rendered inert by the heat of boiling water.

During the mashing process large quantities of raw grain are kept in contact with malt and water at a moderately elevated temperature, whereby the starch by action of the diastase is first changed to maltodextrin and maltose, and finally all converted into dextrose, apparently by the simple appropriation of water, as shown by the following equations:

$$(1)\quad \underset{\text{Starch.}}{4C_6H_{10}O_5} + 2H_2O = \underset{\text{Maltose.}}{2C_{12}H_{22}O_{11}}$$

$$(2)\quad \underset{\text{Maltose.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Dextrose.}}{2C_6H_{12}O_6}$$

The saccharine solution thus obtained is known as wort, and, after addition of some yeast, is allowed to undergo fermentation at a temperature which is maintained between 15° and 30° C. (59° and 86° F.), whereby a weak alcoholic liquid is produced, due to the splitting up of dextrose into alcohol and carbon dioxide: thus, $C_6H_{12}O_6 = 2C_2H_5OH + 2CO_2$. Besides alcohol and carbon dioxide, however, some amyl alcohol and other homologous products, collectively designated as fusel oil, are also produced, and Pasteur has shown that small quantities of glycerin (3 per cent.) and succinic acid (0.6 per cent.) are invariably formed. The composition of these so-called low wines or weak spirits, varies with the starchy material used in their manufacture; thus, potato starch always yields a much larger proportion of amyl alcohol than grain starch, while grain spirit is contaminated with œnanthic and other ethers. The percentage of alcohol in mashed and fermenting mixtures never exceeds 14 per cent., since the yeast plant cannot live in fluid containing a larger percentage.

Distillation of the fermented liquid furnishes a product much richer in alcohol (raw whiskey), which is then further rectified by treatment with recently burned charcoal and subsequent distillation in stills provided with a series of condensers, in the first of which much of the water and amyl alcohol is retained, allowing a purer and stronger alcohol to pass on to the other condensers. For the further removal of water and foreign odors from alcohol, distillation over sodium manganate, anhydrous sodium acetate, and freshly burned lime is employed.

For the purpose of facilitating the rectification of alcohol on a large scale, use is made of a distilling column or dephlegmator, which is interposed between the still proper and the condenser, and, as shown in Fig. 333, consists of a series of communicating chambers, one above the other. The vapor rising from the still enters the lowest chamber through a narrow tube projecting upward into the chamber, and, having filled the space, passes into the next compartment through a second tube situated on the opposite side to that through which the vapor entered. By this arrangement the less volatile vapors will be

condensed, and the resulting fluid collects on the bottom of each compartment, and if in sufficient quantity to rise above the projecting tube it flows into the next lower chamber, thus gradually separating the less volatile vapors from the more volatile, and finally allowing only the more volatile vapor to pass from the uppermost compartment into the condenser. Naturally the continual influx of hot vapor from the still keeps the liquid collecting on the bottom of the several compartments warmed, whereby the more volatile portions are constantly being vaporized and loss thus avoided.

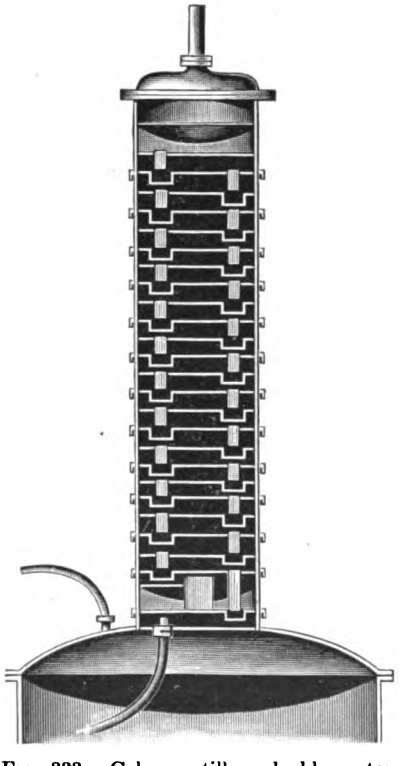


FIG. 333.—Column still or dephlegmator.

During the past fifteen or twenty years alcohol has been successfully produced from cellulose by treating dried peat with very dilute sulphuric acid for several hours at a temperature of 120° C. (248° F.), whereby peat sugar is formed, which is subsequently fermented with yeast and distilled, yielding as much as 62 liters of absolute alcohol for 1000 kilograms of dry peat used (about 15 gallons for each ton).

German and French patents have also been obtained for the manufacture of alcohol from sawdust. The process now in operation consists in first digesting sawdust with water and sulphurous acid, under pressure, in sealed vessels; during the digestion dextrin and other sugars are formed together with acetic acid; the acid having been separated, the converted sawdust is transferred to tanks, where it is neutralized and made into a mash, which is then fermented and distilled, as in the case of alcohol from grain. As much as 30 gallons of 94 per cent. alcohol has been obtained from 3200 pounds of green or 1 ton of dry sawdust. Plants with a capacity of from 50 to 100 tons of sawdust have been erected in Canada and the United States for the manufacture of alcohol by this method.

The Pharmacopœia recognizes three different grades of strength of alcohol, designated by specific names, thus:

	Percentage of True Ethyl Alcohol.	
	By weight.	By volume.
Alcohol . . . . . about	92.3	94.9
Dehydrated alcohol	99.0	99.5
Diluted alcohol . . . . . about	41.5	48.9

Whenever alcohol and water are mixed, heat is evolved and contraction of volume results, both varying with the proportions of the liquids used. According to Flückiger, the rise of temperature will be greatest when 30 parts by weight of absolute alcohol are mixed with 70 parts by weight of water, amounting to 9° C., or 16.2° F., and the greatest contraction occurs when 58 volumes of absolute alcohol are mixed with 54 volumes of water, amounting to a loss of 4 volumes or 3.57 per cent. of the total mixture.

The use of the alcoholometer for ascertaining the percentage strength of commercial alcohol has been fully explained on page 69, and rules have been given on page 80 for preparing weaker alcohol from a stronger variety by dilution with water.

Commercial alcohol does not always come up to the requirements of the Pharmacopœia for official alcohol, averaging, as a rule, from 91 to 93 per cent. by volume of ethyl hydroxide; but the variety sold as *Cologne spirit* generally contains 94.5 or 95 per cent.; the latter is also to be preferred on account of its freedom from foreign odor. Alcohol which has been stored for some time in barrels, particularly if the latter have been imperfectly charred on the inside is apt to be contaminated with coloring-matter and tannin. As found on the market, ordinary alcohol, and even Cologne spirit, frequently has an acid reaction, due to the presence of acetic acid, derived from the aldehyde always more or less present. It is therefore necessary to redistil such alcohol from potassium hydroxide or lime before using it for analytical purposes, especially the titration of alkaloids.

Since alcohol may be adulterated with methyl alcohol, the Pharmacopœia gives a special test for detection of the latter, as follows: Dilute the alcohol with distilled water so that the liquid shall contain about 10 per cent. of absolute alcohol. Transfer 5 mils. (or Cc.) of the diluted alcohol to a test tube, add to it 2 mils. (or Cc.) of potassium permanganate solution (made by dissolving 3 Gms. of potassium permanganate in 100 mils. (or Cc.) of distilled water) and 0.3 mil. (or Cc.) of sulphuric acid, and let the mixture stand for 5 minutes. Now dissolve the precipitate of manganese dioxide by the addition of sulphurous acid, drop by drop, with agitation, then add 1 mil. (or Cc.) of sulphuric acid and 5 mils. (or Cc.) of fuchsin-sulphurous acid test-solution and mix. After standing for 10 minutes, a colorless liquid should result, indicating the absence of methyl alcohol.

Dehydrated Alcohol.—This name is now applied to the article formerly recognized in the Pharmacopœia as absolute alcohol, and still so designated in the foreign pharmacopœias. It is identical with official alcohol, as far as the absence of amyl alcohol and other impurities is concerned, but contains less water, the Pharmacopœia not allowing more than 1 per cent. by weight of the latter. The entire absence of traces of moisture is practically impossible, although the amount is reduced to less than 0.5 per cent. by some manufacturers.

Among the various dehydrating agents suggested, freshly burned lime has been found most desirable.

In the manufacture of dehydrated alcohol, high grade commercial alcohol (95 per cent.) free from foreign odor, is either shaken with the lime in coarse powder for some time, or caused to percolate repeatedly through alternate layers of fine and coarse granules of lime, in an apparatus so arranged as to avoid all contact with air, after which it is transferred, without exposure, to a column still and distilled at a low temperature, under reduced pressure, by which means the alcohol vapor is made to pass through several condensing chambers, in which any aqueous moisture still remaining will be separated and flow back into the still.

Dehydrated alcohol is very hygroscopic, and should be preserved in tightly stoppered bottles containing either some anhydrous cupric sulphate or pieces of freshly burned lime. Its specific gravity should not be above 0.790 at 25° C. (77° F.). In pharmacy its use is confined to that of a solvent for phosphorus and similar substances, but in the manufacture of certain chemicals it is more extensively employed.

Diluted Alcohol, a most valuable solvent for many vegetable principles, is made by mixing equal volumes of official alcohol and water. Since the mixture suffers nearly 3 per cent. loss by contraction, this finished, cooled product contains about 48.9 per cent. by volume of absolute ethyl alcohol. It should not be used until the temperature of the mixed liquids has fallen to that of the room.

Proof spirit, as recognized by the U. S. Government, contains 50 per cent. by volume of absolute alcohol, and is reckoned by gaugers as equivalent to 100 degrees; hence, the term 25 or 40 above or below proof does not refer to liquids containing 25 or 40 per cent. of alcohol, more or less, than the 50 per cent. proof spirit but only one-half as much, namely, 12.5 or 20 per cent., each proof degree representing 0.5 per cent. of absolute ethyl alcohol. Official 94.9 per cent. alcohol is thus said to stand at 189.8 degrees, or 89.8 degrees above proof.

Denatured Alcohol.—In 1906 Congress passed a law, which went into effect January 1, 1907, permitting the denaturing of alcohol by adding to it certain prescribed substances which render it unfit for drinking or medicinal purposes, but do not interfere with it for technical uses. Such denatured alcohol is not subject to an internal revenue tax, and can, therefore, be sold at a very low price as compared with tax-paid alcohol. The substances used as denaturants vary with the special purposes for which the alcohol is intended; in some cases methyl alcohol only is added, in others methyl alcohol and benzin or methyl alcohol and pyridine bases, and in still others methyl alcohol, castor oil, and caustic soda lye, etc.

In 1912 the Commissioner of Internal Revenue at Washington, D. C., issued a series of 17 formulas for the preparation of denatured

alcohol to be used for general antiseptic purposes in hospitals and sanitariums, and exempting such alcohol from tax. Alum, tannic acid, carbolic acid, formaldehyde, mercuric chloride, oil of cajuput, oil of gaultheria, zinc sulphate, and compound solution of cresol are the various denaturing agents named for such alcohol.

A fuller account of the subject of denatured alcohol, together with the formulas and combinations approved by the Government, can be found in the *National Standard Dispensary* for 1916, pp. 130–135.

DERIVATIVES OF ALCOHOL.

The following preparations made from ethyl alcohol are officially recognized in the Pharmacopœia, and therefore of special interest to pharmacists: ether, ethyl carbamate, ethyl chloride, spirit of nitrous ether, paraldehyde, hydrated chloral, and iodoform. In addition, a few allied and some unofficial preparations will also be considered.

Ether.—The general term ether is used by chemists to designate oxides of hydrocarbon radicals; both simple and mixed ethers are known, as the oxygen may be united to two groups of the same or mixed radicals; thus, $(C_2H_5)_2O$, ethyl ether, and $(CH_3)_2O$, methyl ether, are simple ethers, while $(CH_3C_2H_5)O$, methyl ethyl ether, is a mixed ether.

The Pharmacopœia recognizes but one compound by the name ether (Latin *æther*), namely, ethyl ether or ethyl oxide, $(C_2H_5)_2O$, and in all official formulas and physicians' prescriptions this substance is to be understood as intended. Ethyl ether is sometimes called sulphuric ether, and several commercial varieties, known as concentrated and washed ether, are occasionally found on the market; but as their strength and purity are not stated on the label, they should not be used in place of the official ether. The process of ether manufacture consists in heating a mixture of alcohol and sulphuric acid in a suitable still, by means of steam coils, to 130° C. (266° F.), and when the distillation of ether begins, allowing a continuous supply of alcohol to fall into the still from a feed-back so regulated that the mixture shall be kept at a constant quantity and temperature. The vapors are passed through two purifiers: the first one, of cast iron, containing a solution of potassium hydroxide, in which water and other impurities are washed out; the second one, of block tin, is provided with a bed of pebblestones, where alcoholic and other vapors having a higher boiling point than ether are recondensed and carried to the feed-back near the still. In order that no ether may be lost, both purifiers are kept heated, the purified ether vapor being finally condensed in a large worm surrounded by running water.

Etherification may be explained thus: When alcohol and sulphuric acid are mixed, one molecule of each combines to form ethylsulphuric acid and water, $C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + H_2O$. In the

presence of heat and an excess of alcohol a further reaction ensues, ether being produced and sulphuric acid regenerated; thus, $C_2H_5HSO_4 + C_2H_5OH = (C_2H_5)_2O + H_2SO_4$.

The theoretical yield of ether amounts to nearly 5 pounds for each gallon of alcohol used, but in practice rarely more than 4 pounds are recovered. It is important that the temperature be kept between 130° and 138° C. (266° and 280.4° F.), so as to avoid the distillation of much alcohol vapor and the formation of other compounds. Since sulphuric acid is continually regenerated its power of etherifying alcohol is theoretically without limit, but in practice it is found that water and other impurities in the alcohol gradually interfere, the acid being diluted and becoming black while the mixture in the still begins to froth. According to the late Dr. Squibb, a charge of 360 pounds of concentrated sulphuric acid is sufficient for the etherification of 120 barrels of good, clean alcohol.

In order to reduce the cost of production manufacturers of ether for anæsthesia, since 1908, are using, with special permission of the government, alcohol previously mixed with 10 per cent. by volume of ether, and thus avoid payment of the usual internal revenue tax on the alcohol, since alcohol thus mixed under government supervision for the specific purpose indicated is considered as denatured alcohol.

Official ether has a specific gravity of 0.713 to 0.716 at 25° C. (77° F.) and contains about 96.5 per cent. (not less than 95.5 per cent., nor more than 97.5 per cent., U. S. P.), of absolute ethyl oxide; the remaining 3.5 per cent. consists of alcohol and traces of water which it is impracticable to remove. It is best preserved in tin containers holding from 100 Gms. upward, as they are less liable to breakage than glass. Ether is very inflammable, and its vapor, which is about two and a half times as heavy as air, when mixed with the latter explodes in contact with flame; hence care is necessary in handling and dispensing ether, especially at night.

The Pharmacopœia demands the absence of peroxides in ether, as determined by shaking 10 mils. (or Cc.) of ether occasionally during one hour with 1 mil. (or Cc.) of freshly made 10 per cent. solution of cadmium and potassium iodide in a glass-stoppered cylinder previously rinsed with the ether under examination and protected from light; no color should develop in either liquid.

Besides being used in various manufacturing processes, ether enters also into the composition of an alcoholic solution, designated in the Pharmacopœia as spirit of ether (see page 290), which should be prepared by the pharmacist himself.

Ethyl Bromide. C_2H_5Br.—This liquid, also known as hydrobromic ether, belongs to the class of compounds called by chemists haloid ethers, the hydroxyl groups in the corresponding alcohols having been replaced by one of the haloid elements. While not official in the United States and British Pharmacopœias, it is recognized in the

German Pharmacopœia as *æther bromatus*, and is prepared by distilling a mixture of potassium bromide, alcohol, and sulphuric acid, washing the distillate with potassium carbonate solution and then water, and finally rectifying over calcium chloride. The following equation explains its formation: $C_2H_5OH + KBr + H_2SO_4 = C_2H_5Br + KHSO_4 + H_2O$. Ethyl bromide is a colorless liquid of nearly the same specific gravity as chloroform, but boiling at 38° or 40° C. (100.4° or 104° F.); it has a neutral reaction, but is readily decomposed by light and air, becoming acid and dark in color. It must not be confounded with *ethylene bromide*, $C_2H_4Br_2$, a liquid of 2.163 specific gravity and boiling at 131° C. (267.8° F.).

Ethyl Carbamate. $C_3H_7NO_2$ **or** $CO.NH_2.OC_2H_5$.—This compound, also known as ethyl-urethane, and commercially usually designated simply as urethane, is an ester of carbamic acid, obtained by the action of alcohol on urea or one of its salts.

In chemistry the general term "urethane" is applied to all esters of carbamic acid, which acid, however, has thus far never been isolated, and is only known in combination: its most familiar compound is ammonium carbamate, $NH_4NH_2CO_2$, one of the constituents of official ammonium carbonate. If the formula for carbamic acid is assumed to be HNH_2CO_2 then the formation of all urethanes may be explained by the substitution of a univalent radical for the one atom of displaceable hydrogen, which may be brought about in various ways.

Ethyl carbamate may be prepared by allowing an excess of alcohol to react with urea nitrate at a temperature of about 125° C. (257° F.) in a sealed tube for several hours. The resulting mass, when cool, becomes crystalline, and is then dissolved in just sufficient water, the solution being subsequently repeatedly shaken out with ether. After recovery of the ether the residue is distilled and recrystallized from water. The reaction involved is shown by the following equation: $(NH_2)_2COHNO_3 + C_2H_5OH = CO.NH_2.OC_2H_5 + NH_4NO_3$.

Ethyl carbamate occurs in colorless, columnar, odorless crystals, which are soluble in less than their own weight of water or of alcohol, at ordinary temperature. It is used as a hypnotic.

Ethyl Chloride. C_2H_5Cl.—A haloid derivative of alcohol, also known as monochlorethane and hydrochloric ether. It may be obtained by passing dry hydrochloric acid gas into cold absolute alcohol, distilling at a very moderate heat, washing the distillate with water and a weak alkaline solution, and rectifying. It is said also to be made on a large scale by heating a mixture of alcohol and concentrated hydrochloric acid for some time under increased pressure (40 atmospheres) at a temperature of 150° C. (302° F.), and then distilling the resulting product. The ethyl chloride vapors are passed through water warmed to 25° C. (77° F.), then dried by passing over calcium chloride, and

finally condensed in well cooled vessels. The reaction between alcohol and hydrochloric acid is shown by the following equation: $C_2H_5OH + HCl = C_2H_5Cl + H_2O$.

Ethyl chloride is a colorless, mobile, very volatile liquid, having a rather agreeable odor. It has a specific gravity of 0.918 at 8° C. (46.4° F.), or 0.921 at 0° C. (32° F.), and boils at 12.5° to 13° C. (54.5° to 55.4° F.), and hence should be kept in sealed glass tubes in a cool place. As it is very inflammable, it should never be used in proximity to fire. In Europe, more especially in Belgium and France, it is used under the names *chelen* and *kelen*. The Pharmacopœia demands the absence of hydrochloric acid and alcohol; the former can be readily detected by adding a few drops of silver nitrate solution to an alcoholic solution of ethyl chloride, when no turbidity should appear.

Ethyl chloride is usually employed as a local anæsthetic, and mixtures of it with other compounds have been introduced for general anæsthesia, such as *anæsthol*, composed of ethyl chloride 17 parts, chloroform 36 parts, and ether 48 parts, all by weight; *somnoform*, composed of ethyl chloride 60 parts, methyl chloride 35 parts, and ethyl bromide 5 parts, all by weight. *Anæsthol* (Speier) is not identical with the preceding, but is a mixture of ethyl chloride and methyl chloride.

Bromoform. $CHBr_3$.—This compound, also known as tribrommethane, belongs to the general group of halogen substitution compounds. It may be obtained by the action of calcium or potassium hypobromite on acetone, the mixture being distilled with the aid of heat. The reaction occurring is shown by the following equation: $C_3H_6O + 3KBrO = C_3H_3Br_3O + 3KOH$; $C_3H_3Br_3O + KOH = CHBr_3 + KC_2H_3O_2$; tribromacetone being formed during the first reaction, and this, reacting with potassium hydroxide, yields bromoform and potassium acetate. The distillate is washed with water, then shaken with sulphuric acid, again washed with water, and finally freed from remaining traces of acid by washing with sodium hydroxide solution; the bromoform thus purified is dehydrated with calcium chloride and carefully distilled, that portion coming over between 148° and 149° C. (298.4° and 300.2° F.) being collected.

The official bromoform is a mixture of about 96 per cent. of absolute bromoform and about 4 per cent. of dehydrated alcohol, the latter being added as a preservative agent. It is a heavy, colorless, mobile liquid, having an ethereal odor and a sweetish taste resembling chloroform; very slightly soluble in water, but soluble in all proportions in alcohol and in fixed oils. It has a specific gravity of from 2.595 to 2.620 at 25° C. (77° F.), and boils at 148° C. (298.4° F.); when cooled to 6° C. (42.8° F.) it solidifies.

The Pharmacopœia demands the absence of acid, brominated compounds, free bromine, and acetone, and gives appropriate tests for the detection of these impurities in distilled water which has been shaken with the bromoform and allowed to separate completely.

Since bromoform is miscible with fixed oils, a very convenient method of dispensing the same would seem to be to mix it with its own or twice its volume of expressed oil of almond and then to emulsify the mixture with acacia and water in the usual manner.

Bromoform is unfit for use if it has become colored or if of an acid reaction, showing decomposition; it should be preserved in dark amber-colored bottles in a cool place, and never be exposed to direct sunlight.

Chloroform. $CHCl_3$.—Like bromoform, chloroform belongs to the halogen substitution compounds, and resembles the former preparation in many respects. Formerly all chloroform was made by distilling alcohol with a mixture of chlorinated lime and water, and the British Pharmacopœia still recognizes this process, with the addition of slaked lime. The reactions by this method are somewhat complicated, resulting in the final formation of chloroform and calcium chloride and formate. By shaking the distillate with water to remove undecomposed alcohol, crude chloroform is obtained.

Chloroform may also be obtained by treating hydrated chloral with sodium hydroxide, when the following reaction occurs: $CCl_3CHO.H_2O + NaOH = CHCl_3 + NaCHO_2 + H_2O$. The chloroform is distilled off, while sodium formate remains in aqueous solution.

Since 1885 nearly all chloroform has been made from acetone by distillation with chlorinated lime, it having been found to be the richest chloroform-yielding substance known. The reaction occurring may be illustrated as follows: $2C_3H_6O + 6CaOCl_2 = 2CHCl_3 + Ca(C_2H_3O_2)_2 + 2Ca(OH)_2 + 3CaCl_2$. The chloroform obtained by this method is quite free from the chlorinated by-products frequently found in that made from alcohol.

For the purpose of purification on a commercial scale, chloroform is made to bubble slowly through two successive deep layers of concentrated sulphuric acid, and afterward brought into intimate contact with anhydrous sodium carbonate for the purpose of removing any water and acid mechanically carried over. Finally, the chloroform is siphoned into a dry still and distilled in a waterbath at a temperature not exceeding 62° C. (142.6° F.). The sulphuric acid destroys any organic impurities present and gradually darkens in color, finally becoming black.

Absolutely pure chloroform is very unstable when exposed to air and diffused daylight; but if air be rigidly excluded, it does not suffer decomposition even in direct sunlight. Experience has proved that the best preservative agent for chloroform is alcohol, and the Pharmacopœia therefore directs the presence of from 0.6 to 1 per cent. of the latter. The chief products of decomposition of chloroform are free chlorine and carbonyl chloride, $COCl_2$, which are readily detected by the official tests, and no chloroform should be used for internal administration which shows any contamination. The present

Pharmacopœia recognizes but one kind of chloroform, but the term "purified chloroform" is still used by some manufacturers.

The term formyl terchloride is sometimes applied to chloroform; it may also be called trichlormethane if looked upon as methane or marsh gas, in which three hydrogen atoms have been replaced by chlorine.

Iodoform. CHI_3.—This compound, also known chemically as triodomethane, and analogous to bromoform and chloroform in chemical composition, is unusually rich in iodine, and may be obtained from alcohol by the action of the former element in the presence of alkali hydroxides or carbonates. It contains about 97 per cent. of iodine. For many years only alcohol was used and either Bouchardat's or Filhol's process employed. The former consists in heating iodine, potassium bicarbonate, alcohol, and water, in a long-neck flask, to between 60° and 80° C. (140° and 176° F.) until the color has disappeared, then adding small portions of iodine as long as these are taken up and decolorized; the mixture is finally set aside for twenty-four hours and the crystals collected on a filter. About one-third of the iodine is recovered as iodoform, the remainder forming potassium iodide.

Filhol's process insures a much larger yield. Iodine is added in small portions to a warm mixture of sodium carbonate, water, and alcohol, and, after cooling, the crystals are collected; the filtrate is again warmed, some alkali carbonate added, and a rapid current of chlorine passed through the liquid as long as iodoform is separated, which is again collected and the filtrate made to yield more iodoform by repeating the treatment. The formation of iodoform may be illustrated by the following equation: $C_2H_5OH + I_8 + 6KHCO_3 = CHI_3 + 5KI + KCHO_2 + 6CO_2 + 5H_2O$, alkali formate being probably always produced, together perhaps with ethyl iodide, acetic ether, and other compounds. The result appears to be greatly influenced by the relative proportions of the materials used and the temperature employed.

Since 1889 the process of Sulliot and Raynaud has largely been used, by means of which iodoform of unusual purity is obtained. A solution of 50 parts of sodium or potassium iodide (in France, derived from the ash of sea weed) is mixed with 6 parts of acetone and a solution of 2 parts of sodium hydroxide in 1000 parts of water; a dilute solution of sodium hypochlorite is added drop by drop as long as iodoform is produced, the yield being about the theoretical quantity according to the equation $3NaI + 3NaClO + C_3H_6O = CHI_3 + 3NaCl + NaC_2H_3O_2 + 2NaOH$.

At present considerable quantities of iodoform are made by subjecting a solution of 50 parts of potassium iodide in 300 parts of water and 30 parts of alcohol to electrolysis, while a constant current of carbon dioxide is passed into the liquid.

At present considerable quantities of iodoform are made by subjecting a solution of 50 parts of potassium iodide in 300 parts of water and 30 parts of alcohol to electrolysis, while a constant current of carbon dioxide is passed into the liquid.

Iodoform occurs in small, lemon-yellow, scale-like crystals, and also in the form of powder, which have a strong characteristic odor, which to most persons is very disagreeable.

While iodoform is soluble in alcohol, ether, chloroform, glycerin and olive oil, it is nearly insoluble in water, although it imparts its odor and taste to the latter when shaken with it, but the filtrate from such a mixture should be colorless and free from a bitter taste and should not affect litmus, showing the absence of trinitrophenol as an adulteration and acids and alkalies as impurities.

The odor of iodoform in mixtures and ointments may be disguised by the addition to 1 ounce of from 3 to 5 drops of oil of peppermint; Peru balsam, cumarin, the oils of fennel, anise, and others, have also been recommended. The odor adheres persistently to the vessels in which preparations of iodoform have been made, but may be removed by a few drops of oil of turpentine, followed by soap and water.

During the past twenty-five years several substitutes for iodoform have been introduced, but, in spite of the persistent unpleasant odor of the latter, its use by physicians still surpasses that of the proposed substitutes, of which the best known is aristol, which is recognized in the Pharmacopœia under the name thymol iodide.

Hydrated Chloral. $C_2HCl_3O + H_2O$ or $CCl_3COH + H_2O$.—This compound, as indicated in the official title, is a combination of chloral and water. Anhydrous chloral is an oily liquid having the composition CCl_3COH.

In the manufacture of hydrated chloral perfectly dry chlorine gas is passed into cold absolute alcohol as long as the former continues to be rapidly absorbed, after which the mixture is rapidly warmed to 60°–70° C. (140°–158° F.) and treated with sulphuric acid, whereby crude chloral is separated as a thin oily liquid, which is then rectified over burned lime and chalk; the final distillate of pure chloral is weighed and hydrated by the addition of a calculated quantity of water, the hot mass being poured upon plates of glass, covered with a bell glass and allowed to crystallize.

The reactions occurring in the above process were at one time supposed to consist in the formation of aldehyde and the conversion of this into chloral or trichloraldehyde by the action of chlorine, as illustrated by the equations $C_2H_5OH + Cl_2 = C_2H_4O + 2HCl$ and $C_2H_4O + Cl_6 = CCl_3CHO + 3HCl$. This view is no longer tenable, since it has been found that chlorine brought into contact with aldehyde yields trichlorbutylaldehyde, $C_4H_5Cl_3O$, a condensation product, instead of chloral. According to later authorities, the nascent aldehyde produced by the action of chlorine on alcohol acts upon the absolute

alcohol present, forming acetal and water; thus, $2C_2H_5OH + C_2H_4O = C_2H_4(OC_2H_5)_2 + H_2O$; the acetal is converted by chlorine into trichloracetal, $C_2H_4(OC_2H_5)_2 + Cl_6 = C_2HCl_3(OC_2H_5)_2 + 3HCl$, and this is decomposed by the hydrochloric acid present into chloral alcoholate and ethyl chloride; thus, $C_2HCl_3(OC_2H_5)_2 + HCl = C_2HCl_3O.C_2H_5OH + C_2H_5Cl$; finally the chloral alcoholate is decomposed by sulphuric acid into chloral, ethyl sulphuric acid, and water, $C_2HCl_3O.C_2H_5OH + H_2SO_4 = CCl_3CHO + C_2H_5HSO_4 + H_2O$. Other decomposition products are also formed in small quantities.

In order further to purify the crystals of hydrated chloral, it is customary for manufacturers to decompose again the hydrate with sulphuric acid, whereby pure chloral is set free, and then rectify, rehydrate, and recrystallize the product.

Hydrated chloral is readily soluble in water, alcohol, ether, chloroform, fixed and volatile oils. Its solutions are incompatible with caustic alkalies, alkaline earths and ammonia, chloroform and formate of the base being produced. While aqueous solutions of hydrated chloral are perfectly neutral when freshly prepared they gradually acquire an acid reaction, but alcoholic solutions remain neutral. If hydrated chloral be dispensed together with concrete volatile oils or phenols, liquefaction takes place and the mixture must be thoroughly triturated, preferbly in a glass mortar, until a homogeneous liquid results.

The Pharmacopœia requires that hydrated chloral shall contain not less than 99.5 per cent. of pure $C_2Cl_3COH + H_2O$, to be determined by adding an excess of normal potassium hydroxide solution to a solution of an accurately weighed quantity of the compound, and, after allowing the mixture to stand for two minutes, to titrate the excess of alkali with normal sulphuric acid. The equation $(C_2Cl_3COH + H_2O) + KOH = KCHO + CHCl_3 + H_2O$ shows that 1 molecule or 165.4 Gms., of pure hydrated chloral requires 1 molecule, or 56.11 Gms., of potassium hydroxide, and hence each mil. (or Cc.) of the normal solution consumed and containing 0.05611 Gm. of potassium hydroxide corresponds to 0.1654 Gm. of $C_2Cl_3COH + H_2O$, and each Gm. of hydrated chloral, if of official quality, will require not less than 6.015 mils. (or Cc.) of normal potassium hydroxide solution.

Chloral has yielded a number of derivative products which are used to some extent. The most prominent of these is

Chloralformamide. $C_3H_4Cl_3NO_2$ or $CCl_3.CH(OH)NH.COH$.—This compound, which is no longer official in our Pharmacopœia, is recognized in the German Pharmacopœia as *chloralum formamidatum*. It is obtained by interaction between anhydrous chloral and formamide $CHONH_2$, a colorless oily liquid produced by dry distillation of urea and ammonium formate, at about 140° C. (284° F.). Chloralformamide occurs in white, lustrous crystals which are slowly soluble in cold water, but are decomposed by water heated to 60° C. (140° F.).

Other compounds, such as *hypnal*, a compound of chloral and antipyrine, *somnal*, a compound of chloral, urethane, and alcohol, *ural* or *uralium*, chloral-urethane, etc., are less important. A full account of these may be found in the *National Standard Dispensatory*, 1916, p. 449.

Closely allied to the official hydrated chloral is *butyl-chloral hydrate*, $C_3H_4Cl_3COH + H_2O$, which is recognized in the British Pharmacopœia, and is in commerce often, although wrongly, called crotonchloral hydrate. It is prepared from ethyl aldehyde by acting upon it with chlorine at a low temperature, —10° C. (14° F.); the mixture is finally subjected to fractional distillation until a product boiling uniformly between 163° and 165° C. (325.4° and 329° F.) is obtained, consisting of trichlorbutylaldehyde or butyl-chloral, which is then converted into the crystalline hydrous variety by addition of water. Butyl-chloral hydrate dissolves sparingly in cold water, but freely in hot water, alcohol, and glycerin. It differs from hydrated chloral in not yielding chloroform with alkalies, but instead dichlorallylene, $C_3H_4Cl_2$.

Paraldehyde. $(C_2H_4O)_3$.—This liquid is a polymeric form of ethyl aldehyde, which latter is an oxidation product of alcohol.

Aldehydes, chemically speaking, are derived from primary alcohols, contain the characteristic group COH, and upon further oxidation yield acids. Ethyl aldehyde or acetaldehyde, C_2H_4O or CH_3COH, commonly known as aldehyde in commerce, is a colorless neutral liquid obtained by distilling a mixture of alcohol, water, sulphuric acid, and manganese dioxide or potassium dichromate; the crude product is dissolved in ether and charged with ammonia gas. The resulting crystals of aldehyde-ammonia, $C_2H_4ONH_3$, are distilled with diluted sulphuric acid and rectified over calcium chloride. By condensation of three molecules of aldehyde one of paraldehyde is formed, $3C_2H_4O = C_6H_{12}O_3$.

The latter is usually prepared by passing gaseous hydrochloric acid into aldehyde at ordinary temperature until the liquid is no longer soluble in an equal volume of water. By repeated freezing and distillation the crude product is purified until it finally all volatilizes at 124° C. (355.2° F.). Paraldehyde is a colorless liquid of strong, but not pungent, odor, soluble in about 8 parts of water at ordinary temperature and miscible in all proportions with alcohol, ether, and fixed and volatile oils. It is usually dispensed in the form of an emulsion, like ether or chloroform.

Closely allied to acetaldehyde is formaldehyde, HCOH, also known as methyl aldehyde and methylene oxide, which bears the same relation to methyl alcohol as acetaldehyde bears to ethyl alcohol. It is a colorless, pungent gas, obtained by oxidation of methyl alcohol vapor mixed with air. The oxidation is effected by bringing the vapor in contact with moderately heated spirals of copper gauze

superficially oxidized. The Pharmacopœia recognizes an aqueous solution of formaldehyde under the Latin title Liquor Formaldehydi, which is also known in commerce as *formalin* and *formol.* The official solution should contain not less than 37 per cent. of formaldehyde, which may be determined volumetrically. The official assay method was first suggested by Blank and Finkenbeiner in 1898 and involves the oxidation of formaldehyde to formic acid at the expense of the hydrogen dioxide added, the acid being neutralized by the alkali hydroxide, and hydrogen being eliminated according to the following reaction: $2HCOH + H_2O_2 + 2KOH = 2HCOOK + 2H_2O + H_2$. Since 2 molecules, or 60.032 Gms., of formaldehyde will yield by oxidation sufficient formic acid to neutralize 2 molecules, or 112.22 Gms., of potassium hydroxide, as shown by the equation above, each mil. (or Cc.) of normal sodium hydroxide solution neutralized by the newly formed formic acid, in the official test, corresponds to 0.030016 (0.03002) Gm. of formaldehyde. Some of the liberated hydrogen, in the nascent state, is probably oxidized by the excess of hydrogen dioxide to form water.

Paraformaldehyde, also known as **Paraform.**—If an aqueous solution, of formaldehyde is boiled, a portion of the gas is volatilized and another portion is polymerized and becomes insoluble, separating as a soft, white, flocculent mass. Different views are held regarding the exact character of the polymerized product and, while the Pharmacopœia assigns the formula $(HCOH)_3$ to the compound, proof seems to be wanting to show that the molecular weight of the substance is three times that of formaldehyde. According to E. Schmidt (Lehrbuch d. pharm. Chemie, 1911) the soft flocculent mass obtained as stated above passes, upon drying, into trioxymethylene $(CH_2)_3$, while others assert that it may be a mixture of double, triple and possibly other polymeric forms of formaldehyde, in which case the formula $(HCOH)_x$ would seem appropriate. Some authorities even state that the correct formula for paraformaldehyde is $(HCOH)_2$. The name trioxymethylene is used as the official title in the French Pharmacopœia and is given as an official synonym in our own.

The Pharmacopœia requires that the official compound shall contain not less than 95 per cent. of $(HCOH)_3$, to be determined by oxidation to formic acid and titration of the latter with normal potassium hydroxide solution, in the manner directed for the assay of formaldehyde (see above). If $(HCOH)_3$ be the correct formula for paraformaldehyde, the following equation $2(HCOH)_3 + 3H_2O_2 + 6KOH = 6KHCO_2 + 6H_2O + H_6$ shows that 2 molecules, or 180.12 Gms., of paraformaldehyde will yield upon oxidation sufficient formic acid to neutralize 6 molecules, or 336.66 Gms., of potassium hydroxide, and hence each mil. (or Cc.) of the normal alkali solution consumed and containing 0.05611 Gm. of potassium hydroxide will correspond to 0.03002 Gm. of pure $(HCOH)_3$. As already stated in connection with

the assay of the official Solution of Formaldehyde, a part of the liberated hydrogen, in the nascent state, is no doubt converted into water by the excess of hydrogen dioxide.

Paraformaldehyde occurs in white, friable masses, or in powder form, and also in form of compressed tablets weighing 0.5 to 1.0 Gm. It is used for purposes of disinfection by being placed in an iron dish or cup and heated, when it splits up into gaseous formaldehyde, and as such becomes active, possessing strong germicidal properties. To remove the disagreeable, pungent vapor remaining in rooms after the use of formaldehyde, ammonia water may be used, which combines with the gas, forming a harmless compound, which has been introduced into medicine and is officially recognized as

Hexamethylenamine. $C_6H_{12}N_4$ **or** $(CH_2)_6N_4$.—This basic compound, the full chemical name of which is hexamethylene tetramine, is also known as *urotropin*, *cystogen*, *formin*, *uritone*, and *aminoform*. It is a condensation product obtained by adding to a strong solution of formaldehyde small successive portions of stronger ammonia water, the mixture being kept well cooled, until an excess of ammonia is indicated by the odor after the solution has stood several hours. The solution is then poured into shallow dishes and allowed to crystallize. The crystals may be further purified by treatment with animal charcoal and subsequent recrystallization. Hexamethylenamine occurs as colorless odorless, crystals having a sweetish taste, and soluble in 1.5 times their weight of water, the solution showing an alkaline reaction toward litmus.

Hexamethylenamine is recognized in the British Pharmacopœia under the title *Hexamine*, and care is necessary to avoid confusion in this country with a line of pharmaceuticals, powder, tablets, elixir, etc., manufactured by the Hexamine Company, of Syracuse, N. Y., in case *hexamine* is called for on British prescriptions.

Several derivatives of hexamethylenamine have been introduced under special names, thus: Hexamethylene-tetramine salicylate, known as *urotropine salicylate* or *saliform;* hexamethylene-tetramine bromethylate, known as *bromalin*, *bromalium*, *bromoformin*, or *bromethylformin;* hexamethylene-tetramine tannin, known as *tannopin* or *tannon;* hexamethylene-tetramine iodoform, known as *iodoformin;* a compound of hexamethylene-tetramine hydrochloride and ferric chloride, known as *ferrostyptin*. Further particulars regarding these preparations may be found in the *National Standard Dispensatory*, 1916, pp. 794 and 795.

Spirit of Nitrous Ether.—The official preparation recognized by this name is an alcoholic solution of ethyl nitrite, $C_2H_5NO_2$, yielding when freshly prepared and tested by the method of assay given in the Pharmacopœia about 4 per cent. of ethyl nitrite.

In the pharmacopœial process of manufacture, which is especially

intended for the pharmacist in making small quantities of the spirit, the first step is the preparation of ethyl nitrite by acting on a solution of sodium nitrite with sulphuric acid in the presence of alcohol. The nitrous acid liberated attacks the alcohol, forming ethyl nitrite and water. The two reactions are indicated by the following equations: $NaNO_2 + H_2SO_4 = HNO_2 + NaHSO_4$; $C_2H_5OH + HNO_2 = C_2H_5NO_2 + H_2O$. The newly formed ethyl nitrite rises as an oily layer to the surface and, after all reaction has ceased, is transferred to a glass separator where it is washed first with plain ice-cold water and then with an ice cold solution of monohydrated sodium carbonate. After careful separation, the ethyl nitrite is freed from water by agitation with anhydrous potassium carbonate and finally mixed with 21 times its weight of alcohol. In order that a large yield of ethyl nitrite may be insured, it is essential that the tube of the separator be allowed to reach nearly to the bottom of the flask containing the alcohol and sulphuric acid mixture, and that the solution of sodium nitrite be allowed to flow into the flask very slowly in drops, the flask being kept thoroughly cold during the reaction. From the above equation it will be seen that 69.01 Gms. of absolute sodium nitrite are capable of yielding 75.05 Gms. of ethyl nitrite, and if the official salt (containing at least 95 per cent. of $NaNO_2$) be used, the 100 Gms. ordered in the official formula should be able to produce at least 103.32 Gms. of ethyl nitrite, which would yield 2273.04 Gms. of the official spirit. In practice there is always some loss, the full theoretical yield being never obtainable, and hence the necessity of ascertaining the exact weight of the purified ethyl nitrite in order to determine the final weight of alcohol to be added. The process is easy of execution and with little care very satisfactory results are obtained. The amount of pure ethyl nitrite recovered may vary from 70 to 80 Gms. from 100 Gms. of sodium nitrite, and, using such apparatus as are generally found in laboratories, with ordinary precaution the author has obtained 78 Gms.

For some time manufacturing chemists have been offering ethyl nitrite in small sealed tubes to be diluted with the necessary quantity of alcohol, so as to make spirit of nitrous ether in small quantities. This plan is very convenient, and decidedly preferable to the purchase of the spirit in bulk, but it must not be overlooked that ethyl nitrite itself, unless absolutely free from water and kept under favorable conditions is apt to undergo decomposition. Pure ethyl nitrite is a thin, pale yellow liquid, having a pungent, ethereal, apple-like odor. Since it boils at 16° C. (60.8° F.), it should be kept in a cool place, and the containers opened with care.

The Pharmacopœia requires that spirit of nitrous ether shall contain not less than 3.5 per cent., nor more than 4.5 per cent. of ethyl nitrite, which is to be determined by gasometric estimation, the nitric oxide obtainable from a weighed quantity of the spirit being evolved and measured over a saturated solution of sodium chloride in a graduated tube or nitrometer (see Figs. 334 and 335). The official method of

assay is based on the suggestions of the late A. H. Allen, of England (1885), and is much simpler than some other methods proposed. The nitrometer is completely filled with the salt solution, including the bore of the glass stopcock, and care must be observed that no air enter while the different liquids are allowed to flow from the cup into the nitrometer; this is best avoided by washing the cup with a few mils. (or Cc.) of alcohol or salt solution after the other liquids have been run into the tube, and allowing 0.2 or 0.3 mil. (or Cc.) of fluid to remain in the cup.

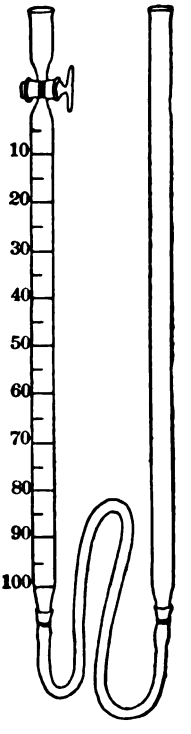


FIG. 334.—Lunge's nitrometer.

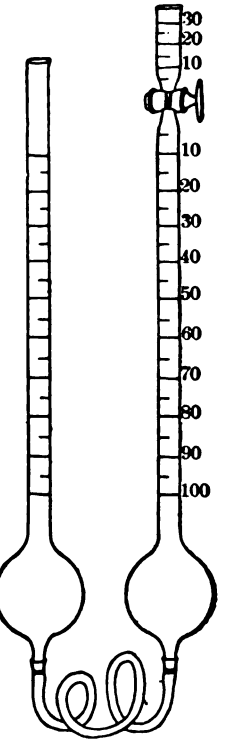


FIG. 335.—Curtman's nitrometer.

The reaction which takes place in the official assay may be shown by the following equation: $C_2H_5NO_2 + KI + H_2SO_4 = C_2H_5OH + KHSO_4 + I + NO$, from which it appears that 30.01 Gms. of NO gas correspond to 75.05 Gms. of ethyl nitrite. At 0° C. (32° F.) and 760 mm. pressure, 1 mil. (or Cc.) of NO gas weighs 0.0013406 Gm., but under the conditions mentioned in the assay method, 25° C. (77° F.) and 760 mm. pressure, it weighs 0.0012281 Gm., and hence the amount of ethyl nitrite corresponding to 1 mil. (or Cc.) of NO gas at the temperature and pressure last mentioned will be found to be 0.0030718 (0.00307127 U. S. P.) Gm., as shown by the following

proportion: 30.01 : 75.05 : : 0.0012281 : x ($x = 0.0030718$). Hence if we let W represent the original weight of spirit of nitrous ether involved in the assay (which must be $\frac{1}{10}$ of the weight of the spirit before dilution to 100 mils. (or Cc.), and N the number of mils. (or Cc.) of NO gas obtained in the assay, then $(N \times 0.0030718) \div W$ represents the weight of absolute ethyl nitrite contained in 1 Gm. of the sample. The amount in 100 Gms. of the spirit or the percentage will be $(N \times 0.0030718 \times 100) \div W$ or $(N \times 0.30718) \div W$, which is the rule given in the Pharmacopœia, where the factor 0.30718 has been rounded off to 0.307.

If the volume of NO gas had a temperature above or below that given in the Pharmacopœia, 25° C. (77° F.), a correction is necessary in the results obtained by the above calculation, the latter applying only to the official temperature. Above 25° C. the volume of NO gas as read is larger than it would be at 25° C., and therefore the per cent. of ethyl nitrite appears greater than is actually true, and a fraction must be subtracted corresponding to the excess of volume of the NO gas over the volume it would have at 25° C. By similar reasoning it follows that when the temperature is below 25° C. a correction must be added corresponding to the deficiency of volume of the NO gas as compared with the volume it would have at 25° C. From Gay-Lussac's law of the relation of gas volumes to their absolute temperatures, the difference between the volume of the NO gas as actually read and what it would be at 25° C. may be calculated. Let t = the temperature at which the NO gas was actually read. Then by the law of expansion 1 mil. (or Cc.) of NO gas at t : x mil. (or C.) at 25° C. : : $273 + t$: $273 + 25$ or $x = \frac{273 + 25}{273 + t}$; that is, 1 mil. (or Cc. of NO gas at t° C. would become $\frac{273 + 25}{273 + t}$ mil. (or Cc.) at 25° C. The correction in volume for each mil. (or Cc.) of NO gas as read at t° C. thus becomes $\left(1 - \frac{273 + 25}{273 + t}\right)$ mil. (or Cc.) $= \left(\frac{t - 25}{273 + t}\right)$ mil. (or Cc.) when it is greater than 25° C., or $\left(\frac{273 + 25}{273 + t} - 1\right)$ mil. (or Cc.) $= \left(\frac{25 - t}{273 + t}\right)$ mil. (or Cc.) when it is less than 25° C. When the temperature is only a few degrees above or below 25° C. the denominator of these fractions is approximately 300, so that they become $\frac{1}{300}$, $\frac{2}{300}$, $\frac{3}{300}$, etc., according as the difference between temperature t of measurement of the NO gas and 25° C. is 1, 2, 3, etc., degrees. As each mil. (or Cc.) of NO gas measured in the assay is too great or too small by $\frac{1}{300}$ part for each degree of temperature above or below the official temperature, fixed at 25° C., it follows that the per cent. as first calculated must be corrected by $\frac{1}{300}$ (*i. e.*, $\frac{1}{3}$ of 1 per cent.), as given in the Pharmacopœia. This correction

deviates more and more from the truth as the temperature difference becomes greater.

If the pressure under which the NO gas is measured is not 760 mm. of mercury, which is the one assumed in the assay formula for calculation, the volume is either too large or too small, and therefore the per cent. of ethyl nitrite found also. If we let p = pressure in mm. of mercury under which the NO gas is measured, then, according to Boyle's law—namely, that the product of the volume and pressure of a gas is always constant, 1 mil. (or Cc.) NO gas $\times p = x$ mil. (or Cc.) NO $\times$ 760, or x = (1 mil. (or Cc.) $\times p$) $\div$ 760—that is, 1 mil. (or Cc.) NO measured at any other pressure, p, would be $\frac{p}{760}$ mil. (or Cc.) at normal barometic pressure, 760 mm. The correction in volume for each mil. (or Cc.) of NO gas measured at pressure p is $\left(1 - \frac{p}{760}\right)$ mil. (or Cc.) or $\frac{760 - p}{760}$ mil. (or Cc.), when p is less than 760, or $\frac{p - 760}{760}$ mil. (or Cc.) when p is greater than 760. When p is greater than 760 the gas is under too great a pressure—that is, the volume is less than it should be, hence a correction should be added to the calculated per cent. as first found in the official method of calculation. When p is less than 760 the correction must be subtracted. According as the pressure is 1, 2, 3, etc., mm. of mercury above or below the normal, 760 mm., the correction for each mil. (or Cc.) of NO gas will amount to 1, 2, 3, etc., times $\frac{1}{760}$, and the correction of the per cent. must be the same number of times $\frac{1}{760}$ of that first found; $\frac{1}{760}$ is sufficiently close to $\frac{1}{750}$ or $\frac{4}{3000}$ of $\frac{1}{1000}$, which means $\frac{4}{3000}$ of 1 per cent. as given in the Pharmacopœia. This correction, as in the case of temperature, is only a close approximation, and must not be construed as absolute.

In place of the gasometric method, volumetric determination of the percentage of ethyl nitrite may be employed, which is readily carried out and is claimed by some to be more accurate than the gasometric estimation. It depends on the interaction of ethyl nitrite with potassium chlorate and subsequent titration of the resulting potassium chloride with silver nitrate, the process being carried out as follows: Into a 100 mil. (or Cc.) flask or bottle of flint glass, pour 10 mils. (or Cc.) of distilled water, 5 mils. (or Cc.) of cold aqueous saturated solution of potassium chlorate, 5 mils. (or Cc.) of spirit of nitrous ether, and 5 mils. (or Cc.) of 10 per cent. nitric acid. Cork quickly and shake the flask or bottle frequently during 30 minutes. Then add 10 mils. (or Cc.) of tenth-normal silver nitrate solution, shake, add 10 mils. (or Cc.) of ferric ammonium sulphate test-solution as indicator, and titrate the excess of silver nitrate solution with tenth-normal potassium sulphocyanate solution. When a permanent reddish color is imparted to the liquid, deduct the number of mils.

(or Cc.) of the potassium sulphocyanate solution required from 10 (the number of mils. (or Cc.) of silver nitrate solution added), multiply the remainder by 2.2515 (0.022515 × 100) and divide the product by the weight of 5 mils. (or Cc.) of the spirit of nitrous ether previously ascertained; the quotient will represent the percentage of ethyl nitrite in the sample. The reactions involved in the preceding method are: $3C_2H_5NO_2 + KClO_3 = 3C_2H_5NO_3 + KCl$; $KCl + AgNO_3 = AgCl + KNO_3$; which show that 3 molecules, or 225.15 parts, of ethyl nitrite are capable of producing 1 molecule, or 74.56 parts, of potassium chloride, and that this in turn requires 1 molecule, or 169.89 parts, of silver nitrate for complete precipitation. Hence each mil. (or Cc.) of tenth-normal $AgNO_3$ solution, containing 0.016989 Gm. of silver nitrate corresponds to 0.022515 Gm. of ethyl nitrite.

It has been shown by previous investigators that aldehyde has no effect on the results obtained by this method, unless it be present in large quantity, in which case it will lower the results.

Whenever an assay of spirit of nitrous ether is to be made, the latter should be carefully neutralized by agitation with potassium bicarbonate before weighing, as free nitrous acid may be present, which would cause the results of the determination to be recorded too high.

Commercial spirit of nitrous ether is often of inferior quality, since it is frequently kept in large bottles and in carboys insecurely stoppered, and consequently becomes oxidized by the air and moisture. It should always be purchased in original packages of small size and preserved in a cool, dark place. The acid reaction observed in some samples of spirit of nitrous ether may be due to acetic acid produced by oxidation of any aldehyde present, or it may be due to decomposition of the ethyl nitrite, resulting in the formation of alcohol and liberation of nitrous acid. Such acidity should invariably be neutralized by means of alkali carbonate before dispensing the spirit in conjunction with alkali iodides, bromides, etc.

Even under favorable conditions spirit of nitrous ether gradually deteriorates, and, if found to contain less than 3 per cent. of ethyl nitrite, should not be sold or dispensed. Freshly prepared spirit of nitrous ether if carefully preserved in a cool, dark place, will keep unchanged for months. Exposure to diffused daylight and air accelerates decomposition; hence, when purchased in bulk, drawn from half-filled or carelessly stoppered containers, the spirit is often worthless. The author has repeatedly had occasion to examine spirit of nitrous ether offered for sale in bulk by jobbers in different parts of the country, and regrets to say that in only a few cases has the strength found approached that required by the Pharmacopœia; in some cases less than 1 per cent. of ethyl nitrite was present.

Pharmacists should make it a rule to keep spirit of nitrous ether in well filled amber-colored containers in a cool place, preferably in 2 ounce or 4 ounce bottles in a refrigerator, so as to avoid the necessity

of frequent opening of the container. *It should never be kept in flint glass bottles, filled or partly filled, on the store shelf, in direct or diffused sunlight.*

Amyl Nitrite.—Under this name the Pharmacopœia recognizes a liquid containing about 80 per cent. of true amyl nitrite, $C_5H_{11}NO_2$, together with variable quantities of undetermined compounds. Although not a derivative of official alcohol, this preparation may be conveniently considered at this point, owing to its similarity, chemically, to ethyl nitrite. Amyl nitrite is an ester, or ethereal salt, bearing the same relation to amyl alcohol as ethyl nitrite bears to official or ethyl alcohol. It can be prepared by direct action of nitric acid on purified amyl alcohol, but is now probably altogether obtained by distilling a solution of sodium nitrite with amyl alcohol and sulphuric acid, that portion of the distillate coming over between 95° and 100° C. (203° and 212° F.) being collected, washed with ice cold sodium carbonate solution, dehydrated with anhydrous potassium carbonate, and redistilled below 100° C. (212° F.). According to the equation $2C_5H_{11}OH + 2NaNO_2 + H_2SO_4 = 2C_5H_{11}NO_2 + Na_2SO_4 + 2H_2O$, 117.10 parts of amyl nitrite should be obtained from 88.10 parts of amyl alcohol, but in practice such is not the case.

As amyl nitrite rapidly deteriorates by exposure to air and light, it must be kept in securely closed, small vials, or in sealed bulbs, in a dark place. The commercial article is very variable in quality, samples having been found to contain as little as 28 per cent. of true amyl nitrite and others containing as much as 93 per cent. The assay of amyl nitrite is directed by the Pharmacopœia to be made gasometrically, as in the case of spirit of nitrous ether, 3 mils. (or Cc.) of the amyl nitrite, which has previously been made perfectly neutral by agitation with potassium bicarbonate and then decanted, being carefully weighed and then diluted with sufficient alcohol to produce exactly 100 mils. (or Cc.) of liquid; of this solution 10 mils. (or Cc.) are used for the assay, representing exactly $\frac{1}{10}$ of the original quantity of amyl nitrite. The volume of gas collected is multiplied by 4.8 (or 0.047851 × 100) and the product divided by the weight of amyl nitrite used in the test ($\frac{1}{10}$ of the weight of the 3 mils. (or Cc.)) to find the percentage. The same corrections for temperature and barometric pressure, as in the case of spirit of nitrous ether, must be made if strictly accurate results are desired.

As in the case of spirit of nitrous ether, amyl nitrite may also be assayed volumetrically by the method described on page 745. Five Gms. of amyl nitrite are dissolved in sufficient alcohol to make 100 mils. (or Cc.) and of this solution 10 mils. (or Cc.) are used for the test. From the equation $3C_5H_{11}NO_2 + KClO_3 = 3C_5H_{11}NO_3 + KCl$ and $KCl + AgNO_3 = AgCl + KNO_3$ it is seen that 3 molecules, or 351.3 Gms., of amyl nitrite will require 1 molecule, or 169.89 Gms., of silver nitrate for precipitation of the potassium chloride formed,

and hence each mil. (or Cc.) of the silver solution consumed in the assay and containing 0.016989 Gm., of silver nitrate corresponds to 0.03513 Gm. of pure amyl nitrite. The number of mils. (or Cc.) of tenth-normal silver nitrate solution required for precipitation in the assay, when multiplied by 3.513 (0.03513 × 100) and then divided by 0.5 (the weight in grams of amyl nitrite used) will express the per cent. of pure amyl nitrite in the sample.

Amyl Alcohol, although not recognized in the Pharmacopœia, is of interest as the source of amyl nitrite and valeric acid and as a valuable solvent used in chemical research. As stated on page 727, amyl alcohol and other homologous products are formed during the fermentation of grain or potato starch; larger quantities may be obtained by continuing the distillation after ethyl alcohol ceases to come over. Amyl alcohol is purified by fractional distillation and repeated washing with a concentrated solution of table salt. It is a colorless, thin, oily liquid of about the same specific gravity as alcohol, but boiling, when pure, at 132° C. (269.6° F.). Chemically, it is amyl hydroxide, $C_5H_{11}OH$, and yields compounds homologous with those of ethyl alcohol, namely, amyl ether $(C_5H_{11})_2O$, amyl aldehyde, $C_5H_{10}O$, and valeric acid, $C_5H_{10}O_2$. Amyl alcohol, obtained in the fermentation of grain or potato starch, is designated by chemists as primary iso-amyl alcohol, and is the chief constituent of commercial fusel oil. It is only slightly soluble in water, but is miscible with alcohol and ether in all proportions.

CHAPTER LVII.

FATS AND FIXED OILS.

THE physical properties of these compounds have been considered on pages 217 to 221. Chemically, they belong to the class of esters, or ethereal salts, being chiefly glycerides of fatty acids, and readily resolved into the respective acids and alcohols by means of alkali hydroxides. The constitution of fats and fixed oils was first studied and announced by Chevreul in 1811. With a few exceptions, the basylous radical is the same for all fats and fixed oils, whether obtained from the vegetable or animal kingdom, namely, glyceryl or propenyl, C_3H_5, a trivalent group derived from the hydrocarbon propane, C_3H_8, the alcohol or hydroxide of which is glycerin or propenyl alcohol, $C_3H_5(OH)_3$; other bases obtainable from fats are myricyl alcohol, $C_{30}H_{61}OH$, cetyl alcohol, $C_{16}H_{33}OH$, ceryl alcohol, $C_{26}H_{53}OH$, cholesterin (from animal fats), $C_{26}H_{43}OH$, phytosterin (from vegetable fats), $C_{26}H_{43}OH$, and others. The acid radicals found in fats are many, the chief ones being arachidic acid, $HC_{20}H_{39}O_2$, butyric acid, $HC_4H_7O_2$, capric acid, $HC_{10}H_{19}O_2$, capronic acid, $HC_6H_{11}O_2$, caprylic acid, $HC_8H_{15}O_2$, cerotic acid, $HC_{26}H_{51}O_2$, erucic acid, $HC_{22}H_{41}O_2$, lauric acid, $HC_{12}H_{23}O_2$, linolenic acid, $HC_{18}H_{29}O_2$, linolic acid, $HC_{18}H_{31}O_2$, melissic acid, $HC_{30}H_{59}O_2$, myristic acid, $HC_{14}H_{27}O_2$, oleic acid, $HC_{18}H_{33}O_2$, palmitic acid, $HC_{16}H_{31}O_2$, stearic acid, $HC_{18}H_{35}O_2$, tiglic acid, $HC_5H_7O_2$, etc., varying from one to three or four in number for a single fat or fixed oil.

The ordinary fats and fixed oils used in pharmacy consist, for the most part, of two or three compound ethers, to which the names olein, palmitin, and stearin have been given; of these, olein, being always liquid, naturally forms the chief constituent of fixed oils, while palmitin and stearin, being solid at ordinary temperatures, by their presence determine the firmer consistence of solid fats. All three are fatty acid esters of glyceryl, known respectively to chemists as glyceryl trioleate, $C_3H_5(C_{18}H_{33}O_2)_3$, glyceryl tripalmitate, $C_3H_5(C_{16}H_{31}O_2)_3$, and glyceryl tristearate, $C_3H_5(C_{18}H_{35}O_2)_3$. The oleic acids derived from different oils, not having a uniform composition and properties, specific names are employed to distinguish the respective glycerides; thus, olein, linolein, and physetolein; the first-named occurs both in animal and vegetable fats, the second only in vegetable fats, while the third is confined to animal fats, chiefly fish oil, seal oil, etc.

When absolutely pure, fats and fixed oils are without action on litmus, but in the presence of air, light, and moisture decomposition and oxidation gradually ensue, an unpleasant odor, due to the for-

mation of volatile products, and an acid reaction being observed. Fats are not affected by a temperature of 100° C. (212° F.) but at 250° C. (482° F.) they are decomposed, various volatile products being formed, among which is an irritating, odorous substance, called acrolein, which chemically, is allyl aldehyde, C_3H_4O or CH_2CHCOH, and is derived from the decomposition of the glycerin present in fats.

Non-drying oils, consisting chiefly of the glyceride of oleic acid, with varying proportions of palmitin, upon exposure to air, appear to absorb water and split up into free oleic (and palmitic) acid and glycerin, the latter being oxidized gradually into carbon dioxide and water, and thus disappearing. The oleic acid absorbs oxygen and is gradually converted into oxystearic acid, and finally into volatile odorous acids, such as capronic, valeric, etc. This process of decomposition is termed rancidification, and explains the condition termed rancidity noticed in old and carelessly preserved fats and fixed oils. By some it is thought that the change is superinduced by the presence of mucilaginous or albuminous matter in the fat, acting as a ferment under the influence of light, air, and moisture. Rancid fats, therefore, when saponified, always contain free acid and yield less glycerin than sweet fats.

In the chemical examination of fats and fixed oils for adulterations, and as tests of identity, two reactions, largely used by analysts, have been adopted by the Pharmacopœia, namely, that with potassium hydroxide and that with iodine. Both tests are applied to every official fat and fixed oil and definite requirements made in connection with the same. In addition the acid value of fats, fixed oils or waxes is frequently determined. The test with potassium hydroxide is better known as the determination of the saponification value or Koettstorfer number, being the number of milligrams of potassium hydroxide required for complete saponification of 1 Gm. of a fat or oil, and is carried out as follows: Weigh out accurately in a flask, holding 150 to 200 mils. (or Cc.), 1.5–2 Gms. of the purified and filtered fat. Next run into the flask from a burette, 25 mils. (or Cc.) of half-normal alcoholic potassium hydroxide solution. While exactly 25 mils. (or Cc.) is not indispensable, in comparative tests precisely the same amount must be used, allowing the burette to drain in exactly the same way in each test. Then place a small funnel in the flask and heat it on a waterbath containing boiling water for ½ hour, so that the alcohol is simmering, frequently imparting a rotatory motion to the contents of the flask. Then add 1 mil. (or Cc.) of phenolphthalein test-solution and titrate back the excess of potassium hydroxide with half-normal hydrochloric acid. If a blank test is made at the same time with the alcoholic potassium hydroxide test-solution alone, the difference in the number of mils. (or Cc.) of half-normal hydrochloric acid consumed by the blank test and the real test, multiplied by 28.055 (being the number of milligrams of KOH contained in each mil. (or Cc.) of the half-normal alcoholic potassium hydroxide solution, which is a half-normal solution)

and divided by the weight in grams of the fat or oil, will give the saponification value of the sample tested. In some cases prolonged boiling is necessary to effect perfect saponification, occasionally 2 or 3 hours being required, and a reflux condenser or long glass tube passing through a cork will be found preferable to a glass funnel for preventing the loss of alcohol.

The test with iodine consists in determining the iodine value or number, which is a figure indicating the number of grams of iodine absorbed by 100 Gms. of a fat or oil under certain conditions. The present official method for determining the iodine number is called the Hanus method and has an advantage over the former method, known as the Huebl method, in that it requires far less time. It is carried out as follows: First prepare a solution of iodine monobromide by dissolving 13.2 Gms. of powdered iodine in 1000 mils. (or Cc.) of glacial acetic acid, using a gentle heat if necessary; cool the solution to 25° C. (77° F.) and determine the iodine content in 20 mils. (or Cc.) of the solution by means of tenth-normal sodium thiosulphate solution; then add to the solution a quantity of bromine equal to that of the iodine present (3 mils. (or Cc.) being the approximate amount), and keep the solution in glass stoppered bottles protected from light. Add to an accurately weighed quantity of about 0.8 Gm. of a solid fat or about 0.3 Gm. of an oil (0.15 to 0.18 Gm. of linseed oil, 0.18 to 0.2 Gm. of codliver oil, and 0.8 to 1.0 Gm. of oil of theobroma), contained in a glass-stoppered bottle of 250 mils. (or Cc.) capacity and dissolved in 10 mils. (or Cc.) of chloroform, 25 mils. (or Cc.) of the iodine monobromide solution, accurately measured from a burette, stopper the bottle securely, and let the mixture stand for half an hour (1 hour is required for castor oil and linseed oil) in a cool place protected from light. After this time it must retain a brown color; if it does not, add another measured portion of the iodine monobromide solution and again set the mixture aside. Then add in the order named 30 mils. (or Cc.) of potassium iodide solution (of the strength of 20 Gms. in 100 mils. (or Cc.)), 100 mils. (or Cc.) of distilled water, and tenth-normal sodium thiosulphate solution in small portions, shaking thoroughly after each addition until the mixture becomes quite pale. Finally add a few drops of starch test-solution and continue the addition of tenth-normal sodium thiosulphate solution until all the color is discharged.

While this test is being carried out, a blank test should be made by mixing exactly the same quantities of iodine monobromide solution and chloroform, and titrating the free iodine as directed above. The difference in the number of mils. (or Cc.) of tenth-normal sodium thiosulphate solution consumed in the blank test and in the actual test when multiplied by 1.2692 (0.012692 × 100) and divided by the weight of the fat or oil taken for the test, gives the iodine number.

The acid value of a fat, fixed oil or wax is the number of milligrams of potassium hydroxide required to neutralize the free acid in 1 Gm.

of the substance. It is determined as follows: Mix 10 Gms. of the substance with 50 mils. (or Cc.) of 90 per cent. alcohol previously neutralized with solution of potassium hydroxide, add 1 mil. (or Cc.) of phenolphthalein test-solution, heat until the fat or wax is melted and titrate with tenth-normal potassium hydroxide solution, shaking constantly. The number of mils. (or Cc.) of tenth-normal alkali solution required, when multiplied by 5.611 (0.005611 × 1000) and divided by the weight of the substance taken, will express the acid value of that particular substance.

The action of acids on fats and fixed oils varies considerably; thus, strong hydrochloric acid has no effect upon them, as also cold diluted nitric acid and cold or hot diluted sulphuric acid. Nitrous acid, as well as warm nitric acid, converts olein into elaidin, a compound isomeric with it, but of firm consistence. Strong sulphuric acid decomposes fats slowly in the cold and rapidly with the aid of heat, forming sulpho-compounds of the fatty acids, as well as of the glycerin. If concentrated sulphuric acid be added to almond or olive oil and the mixture kept at a temperature below 50° C. (122° F.), sulpho-oleic and glycerylsulphuric acids will be formed, $HSO_3C_{18}H_{33}O_2$ and $C_3H_5(HSO_4)_3$; if castor oil be used, sulpho-ricinoleic acid will be produced. The glycerylsulphuric acid upon addition of water is again converted into glycerin and sulphuric acid, and can thus be removed; the sulpho-oleic acid, having been purified by washing with salt solution, can be combined with alkali hydroxides, yielding water-miscible sulpho-oleates, which on account of their absorbability have been recommended as vehicles for ointments, under the names oleite, polysolve, etc. (see page 479).

THE OFFICIAL FATS AND FIXED OILS.

Almond Oil (Expressed).—This oil, usually designated as oil of sweet almond in commerce, is obtained by expression from both bitter and sweet almonds and consists of about 85 per cent. of olein, mixed with palmitin, but is said to be free from stearin, which accounts for the fact that the oil can be cooled to —20° C. (—4° F.) before congealing. Although olive oil, cottonseed oil, lard oil, and sesame oil may be present in commercial almond oil, such is rarely the case now and they can be detected by cooling to —10° C. (14° F.) Formerly peach kernel oil was frequently added to or substituted for expressed oil of almond, but since the enactment of pure food and drug laws this practice has ceased almost entirely, and peach kernel oil is now sold under its own name. The presence of oil of peach kernels and apricot kernels cannot be detected by cooling almond oil, as both oils have nearly the same congealing point. The latter may be detected by mixing almond oil with an equal volume of nitric acid and water, when a white mass free from red color should be obtained; a brown color would indicate the presence of cottonseed and sesame oils.

The saponification value of expressed oil of almond, according to the Pharmacopœia, should be not less than 191 nor more than 200, and the iodine number not less than 93 and not more than 100.

Castor Oil.—The chief constituent of this well known oil is triricinolein, $C_3H_5(C_{18}H_{33}O_3)_3$, together with ricinisolein, palmitin, and dioxystearin. Ricinolein differs from olein in being the glyceride of an acid containing in each molecule one atom more of oxygen than oleic acid. As already stated on page 223, castor oil differs from other fatty oils in its marked solubility in absolute and official alcohol; it is also immiscible with more than its own volume of petroleum benzin or 1½ times its volume of mineral oils. The specific gravity of castor oil, 0.945–0.965 at 25° C. (77° F.), is higher, and its viscosity much greater, than that of any other fatty oil. It is rarely adulterated, although inferior grades of castor oil are to be found on the market; foreign oils may be detected by the appearance of a blackish-brown color if 3 mils. (or Cc.) of the oil be shaken with 3 mils. (or Cc.) of carbon disulphide and 1 mil. (or Cc.) of sulphuric acid, also by the lesser solubility of the oil in alcohol. Although castor oil is usually classed among the drying oils, it only becomes thicker when exposed to the air, but never dries completely, even when exposed in thin layers. It becomes turbid when cooled to 0° C. (32° F.), and even deposits crystalline flakes, but does not congeal until a temperature of —18° C. (—0.4° F.) is reached.

The saponification value of castor oil is given by the Pharmacopœia as not less than 179 nor more than 185, and the iodine number as not less than 83 nor more than 88; the latter is remarkably constant and is given by several authorities as 82–84.

In connection with castor oil mention may be made here of two other constituents of castor beans or seeds, which are interesting on account of their poisonous character. Ricin, an unorganized ferment belonging to the group of toxalbumins, is present in the seeds to the extent of 2.8–3 per cent., and may be extracted from fresh decorticated seed, freed from oil by strong expression, by percolation with a 10 per cent. sodium chloride solution, in which it is soluble. By saturating the percolate with magnesium and sodium sulphates, ricin is precipitated and may be freed from the crystalline salts by dialysis. It is insoluble in alcohol, ether and chloroform, and, although not affected by dry heat, it loses its toxic properties when its solution is heated. Ricinine, a poisonous base, has been found to exist in the seed coats of the castor bean to the extent of 0.15 per cent., and 0.03 per cent. in the oil cake left after expression of the oil. It is extracted with boiling water, the solution evaporated to dryness and extracted with alcohol. Ricinine is soluble in water, alcohol, ether and chloroform. Its solutions are precipitated by mercuric chloride and by iodized potassium iodide solution, but other alkaloidal reagents are without effect. It is not capable of forming salts with acids, and when

treated with sodium hydroxide solution yields methyl alcohol and a dibasic acid named ricinic acid. Recent investigators have assigned the formula $C_8H_8N_2O_2$ to ricinine.

Codliver Oil.—The composition of codliver oil is largely affected by the method and care taken in its extraction and subsequent treatment. It is primarily a mixture of glycerides of stearic, palmitic, jecoleic and therapic acids, and a notable percentage of volatile fatty acids. Cholesterin has been found as a constant constituent, the quantity varying from 0.46 to 1.32 per cent. The first oil exuding from the livers contains less of the organic bases found in codliver oil, while the putrefactive changes which the livers undergo in some cases before expression, no doubt contribute to the development of ptomainic bases found in some varieties of oil. Among the bases thus far identified are the non-volatile morrhuine, $C_{19}H_{27}N_3$, and aselline, $C_{25}H_{32}N_4$, and the volatile bases trimethylamine, butylamine, amylamine, hexylamine, etc. Phosphorus and iodine have also been found in codliver oil in very small quantities. The so-called fish stearin, obtained as a residue when the frozen oil is expressed, is not true tristearin, but, according to Heyerdahl, consists of a mixture of 20 per cent. of glycerides of saturated fatty acids and 80 per cent. of glycerides of unsaturated fatty acids; the exact character of these unsaturated fatty acids has not been determined.

Codliver oil is said to be sometimes adulterated with seal oil and with the oils of menhaden and other fish, for the detection of which the Pharmacopœia gives appropriate tests. According to Gane, seal oil is best distinguished by the very disagreeable odor of the soap obtained by boiling some of the oil with alcoholic potassium hydroxide solution, codliver and other fish oils yielding a soap of only slight herring-like odor. An important test for the quality of codliver oil is the determination of the free fatty acids, which should not exceed 0.3 to 1 per cent.

The Pharmacopœia requires that codliver oil shall show a saponification value of not less than 180 nor more than 190 and an iodine number not less than 140 nor more than 180.

Cottonseed Oil.—This oil consists chiefly of olein, palmitin, and linolein, together with small quantities of the glycerides of linolenic acid and coloring matter, which latter is removed by bleaching the oil with warm weak solutions of alkali hydroxide. Cottonseed oil when saponified with alcoholic potassium hydroxide solution should show a saponification value of not less than 190 nor more than 198. The Pharmacopœia gives the iodine number as not less than 105 nor more than 114. The presence of cottonseed oil in other oils may be detected by Halphen's test and the test with silver nitrate, as explained under Lard, on page 755. Nitric acid of 1.375 specific gravity produces a deep brown coloration with cottonseed oil, the coloration

being more or less vitiated, however, if the oil has been heated to 240° C. (464° F.).

Croton Oil.—The composition of croton oil is very complex, the glycerides of not less than 10 acids having been found—namely, of oleic, palmitic, stearic, myristic, lauric, valeric, formic, butyric, acetic, and tiglic acids, besides which crotonoleic acid, as yet but little studied, is said to be present both in the free and combined state; this latter acid differs from oleic acid in that its barium salt is soluble in alcohol. The vesicant principle of croton oil was determined in 1895 by Dunstan and Boole, of England, and found to be a bright yellow, hard, brittle, substance, to which they gave the name croton resin, and which has the composition $C_{13}H_{18}O_4$; it is soluble in alcohol, ether, and chloroform, and possesses neither acid nor basic properties. Croton oil differs from other non-drying oils in not solidifying either completely or partially when shaken with an equal volume of a mixture of fuming nitric acid and water, and allowed to stand for 24 hours, and from castor oil in its perfect solubility in petroleum benzin. Its saponification value is given by the Pharmacopœia as not less than 200 nor more than 215, and its iodine number as not less than 104 nor more than 110.

Lard.—The most important constituents of lard are olein, about 60 per cent. and stearin, about 40 per cent., together with small and variable amounts of palmitin. Lard sometimes contains free fatty acids, but these are limited by the Pharmacopœia by the test that 10 Gms. of the lard dissolved in chloroform shall not require more than 2 mils. (or Cc.) of tenth-normal potassium hydroxide solution to produce a pink color, phenolphthalein being used as an indicator.

The presence of cottonseed oil is officially detected by means of an alcoholic solution of silver nitrate acidulated with nitric acid, when no reddish or brown color should be observed. In addition to this test Halphen's test should be applied, which consists in mixing melted lard with an equal volume of a mixture of amyl alcohol and a 1 per cent. solution of sulphur in carbon disulphide, and then heating the mixture for 15 minutes in a bath of boiling salt water, when no reddish color should be developed. According to L. Tolman, the test is made more reliable by continuing the heat for 1 or 2 hours.

As lard is sometimes adulterated with beef suet, the Pharmacopœia directs detection of the latter by a microscopic examination of the crystals obtained by setting an ethereal solution of lard aside for 12 hours at a temperature of 20° C. (68° F.) in a test tube loosely closed with absorbent cotton; the resulting crystals, if pure lard stearin, consist of plates cut off obliquely at one end and in irregular groups, whereas beef stearin crystallizes in the form of cylindrical rods or needles with sharp ends and grouped in clusters.

The saponification value of lard is officially given as not less than

195 nor more than 203, and the iodine number as not less than 46 nor more than 70.

Linseed Oil.—While linseed oil contains small proportions of olein, palmitin, myristin, and stearin, it consists chiefly of the glycerides of linolic acid, $HC_{18}H_{31}O_2$, and linolenic acid, $HC_{18}H_{29}O_2$. Formerly, the name linoleic acid was applied to the fatty acid present in largest amount, but this has been shown to be a mixture of oleic, linolic, linolenic, and isolinolenic acids. Upon exposure of linseed oil to the air, oxidation takes place and oxylinolein is formed, producing a hard varnish-like residue. Since pure linseed oil requires several days for perfect drying, its siccative properties are increased by boiling the oil and by addition of lead oxide, manganese oxide and similar substances. The glyceride of oleic acid present in linseed oil behaves like that of the non-drying oils when the oil is exposed to air, but decomposition is probably estopped by the formation of the other oxidation products; hence the acidity and unpleasant odor due to rancidification are not observed. As already stated on page 224, boiled linseed oil should never be used for pharmaceutical purposes.

Linseed oil has been found adulterated with rosin oil and mineral oils, which will remain as an oily residue if the oil is saponified with alcoholic solution of potassium hydroxide; the resulting soap must be completely soluble in water. The Pharmacopœia gives the saponification value of linseed oil as not less than 187 nor more than 195, and the iodine number as not less than 170; the latter is rarely below 175 and varies with oils from different sources, sometimes running as high as 190 and even 198.

Olive Oil.—This oil consists of about 72 per cent. of liquid glycerides (a mixture of olein, 94 parts, and linolein, 6 parts) and about 28 per cent. of solid glycerides, chiefly palmitin with small quantities of arachin. The unsaponifiable matter met with in olive oil has been shown to be phytosterin, and the greenish color of the oil is due to chlorophyl from the olive fruit. Olive oil has been found adulterated with cottonseed and sesame oils, for the detection of which the Pharmacopœia gives appropriate tests. According to Tolman, olive oil contains an impurity which interferes with the tests for cottonseed and sesame oils, and hence all olive oil should first be thoroughly shaken with hot alcohol and then washed with hot water before the official tests are applied. The same authority recommends that during the application of Halphen's test (see under Lard, page 755), the heat should be continued for 1 or 2 hours, as cottonseed oil which has been heated will respond to this test only after 1 or 2 hours, and would escape detection during the short period directed in the official test.

At one time olive oil was grossly adulterated with peanut oil, and the latter even wholly substituted for it; its detection is more difficult

than that of other oils, since its chemical and physical constants are very similar to those of olive oil. The test used by the Bureau of Chemistry of the Agricultural Department at Washington, D. C., which depends upon the determination of arachidic acid, and is given in detail in the *National Standard Dispensatory*, 1916, p. 1151, is said to yield very satisfactory results; 20 times the weight of arachidic acid obtained will approximately indicate the amount of peanut oil present.

The Pharmacopœia gives the saponification value of olive oil as not less than 190 nor more than 195, and its iodine number as not less than 79 nor more than 90.

Sesame Oil.—Benne oil or teel oil, by which names this oil is also known, is obtained by expression, preferably cold, from the seed of the cultivated benne plant, to the extent of from 45–55 per cent. The possible presence of cottonseed oil, as an adulteration, may be readily detected by the Halphen test (see under Lard, p. 755). A characteristic reaction of sesame oil, distinguishing it from other oils is that known as the Baudouin test, which consists in shaking the oil with ten times its volume of hydrochloric acid containing 1 per cent. of sugar in solution for ½ minute; the acid layer will assume a crimson color. The Pharmacopœia gives the saponification value of sesame oil as not less than 188 nor more than 193, and the iodine number as not less than 103 nor more than 112.

Oil of Theobroma.—Cacao butter, by which name this oil is better known, is composed of the glycerides of oleic, stearic, palmitic, and lauric acids, together with small quantities of the glycerides of butyric, formic, linolic, and arachidic acids. A peculiar feature of oil of theobroma is that the specific gravity of recently melted and congealed oil is lower than the normal, the maximum specific gravity not being attained for some time after (from 1 to 3 weeks).

The most probable adulterations of oil of theobroma are wax, stearin, and tallow, for the detection of which the official test with solution in ether is admirably adapted. Under the conditions named in the Pharmacopœia, a solution of pure oil of theobroma will not become turbid or separate granular flocculi in less than 3 minutes and form a clear liquid again at 15° C. (59° F.).

Oil of theobroma, if pure, has a saponification value of not less than 188 nor more than 195, and its iodine number should be not less than 33 nor more than 38.

Spermaceti.—Although composed chiefly of cetyl palmitate, spermaceti contains also glycerides of lauric, myristic, and stearic acids, and is therefore more nearly related to the true fats than wool fat and beeswax. The cetyl palmitate may be separated from the glycerides by recrystallization from alcohol, and when thus purified will not yield vapors of acrolein when heated strongly, whereas ordinary

spermaceti does give off the characteristic irritating vapors due to decomposition of glycerin. Spermaceti is readily saponified by means of alcoholic solution of potassium hydroxide, the resulting liquid yielding cetyl alcohol upon addition of water, It is not usually adulterated, since the addition of other fats would materially alter its physical properties, and detection thus not be difficult. The complete solution of spermaceti in boiling alcohol would show the absence of paraffin.

Suet.—Mutton suet, according to Chevreul, consists of 70–80 per cent. of stearin and palmitin, and 20–30 per cent. of olein, together with a trace of hircin, which latter is the glyceride of hircic acid, having a strong acid reaction and a peculiar goat-like odor. The Pharmacopœia recognizes only the prepared or purified suet (see page 221), and gives the saponification value as not less than 193 nor more than 200, and the iodine number as not less than 33 nor more than 48.

Wax.—Beeswax, which is the only kind of wax officially recognized, is a mixture of myricyl palmitate and free cerotic acid, and is said to contain also ceryl palmitate and free melissic acid. It is subject to adulteration with tallow, Japan wax, rosin, paraffin, and ceresin, all of which can be detected by the tests given in the Pharmacopœia. Pure beeswax contains no glycerides, and hence yields no glycerin. The saponification value of yellow wax is generally given as 90–96; in pure wax this is rarely found below 95. Experience has shown that in the saponification test for wax, from $1\frac{1}{2}$ to 3 hours' boiling is required to effect perfect saponification. A sample of wax thus treated, which after $1\frac{1}{2}$ hours' time showed a saponification value of 65, after 3 hours gave a value of 94.08, and the longer time would therefore seem perferable for all tests of wax in order to secure accurate results.

The Pharmacopœia has adopted the method first suggested by Hager for determining the specific gravity of wax, by ascertaining the specific gravity at 25° C. (77° F.), of a mixture of alcohol and water in which globules of the wax, carefully prepared as officially directed, will float indifferently; it should be from 0.950 to 0.960. The acid value (see page 751) of white wax is given as not less than 17 nor more than 23, and of yellow wax as not less than 18 nor more than 24. The ester value, obtained by boiling melted wax with half-normal alcoholic potassium hydroxide solution for 2 hours and titrating the excess of alkali with half-normal hydrochloric acid, should not be less than 72 nor more than 78 for white wax, and not less than 72 nor more than 77 for yellow wax.

Wool Fat.—Natural wool fat is more closely related to the group of waxes than to that of true fats. It is a complex mixture of free fatty acids, palmitic and cerotic acid esters of cholesterin, isocholes-

terin, and ceryl alcohol, and non-saponifiable bodies, but contains no glycerin. The purified or official fat is obtained, as already stated on page 222, by treatment of the natural fat from wool with weak alkali solution, subsequent washing with water, precipitation with calcium chloride, dehydration with lime and extraction with acetone. After distillation of the solvent, the purified fat thus obtained consists chiefly of cholesterin esters, and should be free from alkalies and free fatty acids. The Pharmacopœia also demands the absence of nitrogenous matter, as shown by boiling wool fat with potassium hydroxide solution, when no vapors of ammonia should be given off, as well as the absence of glycerin and soluble oxidizable impurities, and gives the iodine number of wool fat as not less than 18 nor more than 28.

A characteristic test for the cholesterin esters present in wool fat is Liebermann's cholestol reaction: 1 Gm. of the fat is dissolved in 3–4 Cc. of acetic anhydride, not anhydrous acetic acid, and 6 drops of concentrated sulphuric acid gradually added, when a pink coloration will appear, changing to green or blue.

Saponification.—Alkali hydroxides and moist metallic oxides, in the cold, only partly decompose fats and fixed oils, forming emulsions with them, as shown in the case of the official ammonia and lime liniments; but at boiling temperature complete dissociation is effected, the fatty acids combining with the metallic base, while glycerin is liberated. The new compounds thus obtained are known as soap, and the process is termed saponification; the character of the soap depends upon the particular hydroxide employed, sodium hydroxide invariably forming hard soap, while potassium hydroxide and ammonia form soft soap. The process of saponification may be illustrated by the following equation $C_3H_5(C_{18}H_{33}O_2)_3 + 3NaOH = 3NaC_{18}H_{33}O_2 + C_3H_5(OH)_3$, which represents the manufacture of hard soap from olive oil.

In the manufacture of soap it is customary to add the alkali solution in slight excess to the fat, in order to insure complete decomposition of the latter, the excess remaining in solution. Boiling of the mixture is continued until it becomes transparent and somewhat tenacious, showing that no uncombined fat remains; this is necessary, as the decomposition of the fat is gradual, and the newly formed soap serves as an emulsifying agent for the fat. As the process nears completion iridescent bubbles are seen to rise on the surface, consisting of soap solution. Finally, common salt is added to the finished solution, whereby the soap is precipitated, and can then be drained and allowed to dry in suitable moulds. This explains the fact that ordinary soap will cause no lather with sea water, a special soap made with cocoanut oil or rosin, and known as *marine soap*, being preferable for this purpose, since it is soluble in solution of salt. Since all fats contain some palmitin or stearin (even the fixed oils), the consistence of the soap will depend in part upon the proportion of solid

fats present, being firmest in soaps made partly with stearin fats, such as suet, tallow, etc.

The term saponification is used also to express the decomposition of fats and fixed oils by water with the aid of superheated steam, which results in liberation of the fatty acids and glycerin, as in the case of tallow or suet; thus, $C_3H_5(C_{18}H_{33}O_2)_3 + 3H_2O = 3HC_{18}H_{33}O_2 + C_3H_5(OH)_3$. Chemists, not confining the process to the glycerides of fatty acids, further apply the term to the resolution of all compound ethers by an alkali into the respective acids and alcohols, which is often practised in connection with the determination of certain constituents of volatile oils. The action of potassium hydroxide on aldehyde, resulting in the formation of aldehyde-resin, has also sometimes, but erroneously, been called saponification. In pharmacy the term soap is always restricted to the alkali salts of fatty acids, obtained by treatment of a fat or fixed oil with a boiling solution of sodium or potassium hydroxide, which are soluble in water; the name oleate or plaster is more properly applied to those soaps which are insoluble in water or alcohol and are made with the oxides of the earths or heavy metals. Soap made wholly from animal fat is but sparingly soluble in cold alcohol, and is therefore to be preferred for the preparation of solid opodeldoc and similar firm liniments. Such a soap is recognized in the British Pharmacopœia as *Sapo Animalis* or *Curd Soap.*

Medicated Soaps.—While soaps intended simply as detergents may, without detriment, contain a very slight excess of alkali, it is desirable when medication of the soap is intended, that prior to its application a perfectly neutral substance be employed; it has, in fact, been found that soap containing uncombined fat is even preferable to neutral or normal soap, for not only does it render the skin softer, but reaction between the soap and any medicinal agent added is also thereby avoided or at least retarded. Such soaps, containing an excess of fat, are known as *superfatted soaps*, and have been largely used for the past 25 or 30 years. In preparing them it is customary to add an excess of 3 or 5 per cent. of fat or fixed oil in the beginning of the operation, which then remains intimately mixed with the newly formed soap. In a few cases the excess of fat has been incorporated with the freshly made, neutral soap while yet in a soft, pasty condition. Both olive oil and lanolin are used in the manufacture of superfatted soaps, having been found preferable to all other fats in their action on the skin and toward chemicals.

In the manufacture of medicated soaps the plan followed is identical with that prescribed on page 481 for ointments. The medicinal agent is first intimately mixed (either in the form of solution or impalpably fine powder) with a small portion of the superfatted soap, by means of suitable apparatus, which mixture is then added to such a further quantity of the same vehicle as may be necessary to establish the required percentage strength of the finished product. Among

the various medications of superfatted soaps are tar 5 per cent., sulphur 10 per cent., salicylic acid 5 per cent., borax 5 per cent., carbolic acid 5 and 10 per cent., corrosive sublimate 0.1 and 0.5 per cent., camphor 5 per cent., and others.

Official Soaps.—The Pharmacopœia recognizes two varieties of soaps: one by the general name *soap* (Latin, *sapo*), and the other by the general name *soft soap* (Latin, *sapo mollis*). The first is intended to be a hard soap made from olive oil and sodium hydroxide, as already explained. When fresh, or if kept in a damp cellar, it usually contains a large proportion of water, most of which is driven off by drying in a warm, airy room, and all of which can be expelled at a temperature of 110° C. (230° F.).

The Pharmacopœia limits the moisture content in soap to 36 per cent. for unpowdered soap and to 10 per cent. for powdered soap, and demands the absence of more than 1 per cent. of matter insoluble in hot alcohol. It also requires that the well washed and dried fatty acids, obtained by decomposing a hot solution of soap with diluted sulphuric acid, shall have an iodine number of not less than 84 nor more than 90.

The soft soap of the Pharmacopœia is directed to be made by the action of potassium hydroxide on cottonseed oil. Commercially, it is sometimes designated as green soap, which was formerly also the official title; the color is, however, by no means green, being yellowish brown. The quantity of potassium hydroxide directed in the official formula is based on the assumption that it contains 85 per cent. of absolute KOH; potassium hydroxide of any other strength may be used, and the exact quantity ascertained by dividing 7310 by the percentage of pure KOH contained therein. If p be allowed to represent the unknown percentage, and x the unknown quantity, then $p : 85 :: 86 : x$, and $x = 86 \times 85$ (or 7310) $\div p$.. The Pharmacopœia limits the water content of soft soap to 50 per cent., and requires that the free alkali present shall be not less than 0.1 per cent. nor more than 0.25 per cent. of potassium hydroxide. In the German Pharmacopœia this soap is known as *sapo kalinus*.

Glycerin.—As already stated, the basylous radical found in all true fats and fixed oils, both of vegetable and animal origin, is glyceryl, the hydroxide of which is glycerin, $C_3H_5(OH)_3$, a triatomic alcohol. It has proved a most valuable solvent and preservative in pharmacy, second only to alcohol in this respect. Nearly all glycerin now produced in this country is made by decomposing fats in large copper digesters; fat and water having been put into the digester, steam under 120 to 150 pounds pressure is introduced for several hours, whereby the mixture is kept in constant agitation and the fat is completely decomposed, the glycerin entering into solution in the water, and the non-volatile fatty acids floating on the surface of the aqueous solution.

The volatile fatty acids are allowed to escape with steam through a small orifice in the top of the digester. The dilute solution of glycerin is transferred to evaporating tanks and concentrated until it reaches a density of 28° Baumé, equal to a specific gravity of 1.24 at 15° C. (59° F.). The crude dark amber-colored glycerin thus obtained is introduced into specially constructed stills, into which steam enters at a temperature of about 250° C. (482° F.), carrying the glycerin, in the form of vapor, with steam, over into a series of condensers so arranged that the glycerin condenses in passing through at various degrees of density; the first condenser, being least cooled, contains the heaviest glycerin, the distillate becoming gradually weaker, until in the last condenser almost pure water is collected. Coloring matter is removed by treatment with animal or vegetable charcoal, and the distillation is repeated two or three times until the required degree of purity has been obtained. The Pharmacopœia demands at least 95 per cent. of absolute glycerin, which liquid has the specific gravity of 1.249 at 25° C. (77° F.), and is soluble in water and alcohol in all proportions, as also in a mixture of 3 parts of alcohol and 1 part of ether, but is insoluble in ether, chloroform, benzene, petroleum benzin, fixed and volatile oils. The most important tests of those mentioned in the Pharmacopœia are: the absence of turbidity and color when glycerin, after dilution with water, is mixed with silver ammonium nitrate test-solution and then allowed to stand, protected from light, for five minutes; the absence of an offensive or acidulous odor when glycerin is heated with diluted sulphuric acid; the absence of a color darker than yellow, when a mixture of equal volumes of glycerin and concentrated sulphuric acid is allowed to stand for 1 hour; and the complete volatility of glycerin upon ignition. Although official glycerin boils at about 165° C. (329° F.), it is readily vaporized from an aqueous solution at 100° C. (212° F.).

While glycerin is unaffected by cold nitric or sulphuric acid separately, a mixture of the two acids forms with it a definite chemical compound, glyceryl or propenyl trinitrate, $C_3H_5(NO_3)_3$, commonly but wrongly called nitroglycerin, and known also as glonoin and trinitrin. Glyceryl trinitrate is prepared by adding a mixture of 100 parts of anhydrous glycerin and 3 parts of sulphuric acid (spec. grav. 1.835), gradually and in small portions at a time, to a well chilled mixture of 280 parts of nitric acid (spec. grav. 1.5) and 300 parts of sulphuric acid (spec. grav. 1.835), the vessel being kept surrounded by ice. This mixture is afterward poured into six times its volume of cold water, washed free from acid, and finally dried over sulphuric acid. The reaction may be illustrated as follows: $C_3H_5(OH)_3 + 3HNO_3 + H_2SO_4 = C_3H_5(NO_3)_3 + 3H_2O + H_2SO_4$, the sulphuric acid simply serving to withdraw the water eliminated in the formation of the compound ether. The product is a slightly yellowish, oily liquid, insoluble in water but soluble in alcohol. It has a sweet, aromatic taste, and is very poisonous. In the form of a 1 per cent.

alcoholic solution glyceryl trinitrate is recognized in the Pharmacopœia as *Spiritus Glycerylis Nitratis*—Spirit of Glyceryl Trinitrate, or Spirit of Nitroglycerin; tablet triturates and chocolate tablets containing 0.00065 and 0.0013 Gm. ($\frac{1}{100}$ and $\frac{1}{50}$ grain) of glyceryl trinitrate each are also used by physicians; mixed with three parts of infusorial earth (kieselguhr), it constitutes dynamite, a well known blasting agent.

Glycerophosphoric acid or glycerin acid phosphate, $C_3H_5(OH)_2H_2PO_4$, is another derivative of glycerin introduced into medicine and pharmacy within recent years. It is chiefly used in the form of calcium, iron, or sodium salts. The commercial acid is a 20 per cent. aqueous solution, as all efforts to concentrate the solution and obtain the pure acid have failed, and always resulted in decomposition. When glacial phosphoric acid is gradually dissolved in an equal weight of 95 per cent. glycerin with the aid of moderate heat and the solution then heated in a paraffin bath for several hours at 100°–110° C. (212°–230° F.), water is split off and a new compound results in the form of a tenacious mass, which is then dissolved in water and neutralized with milk of lime or solution of barium hydroxide. Some calcium phosphate (or barium phosphate) will deposit, and is removed by filtration. The remaining solution is concentrated in a vacuum apparatus, and upon addition of alcohol the glycerophosphate is precipitated and then freed from adhering glycerin by washing with alcohol. For obtaining the commercial acid, the barium glycerophosphate is decomposed with a calculated quantity of diluted sulphuric acid and the resulting barium sulphate removed by filtration.

Petroleum Products.—Pharmaceutically closely allied to the fats, but chemically entirely distinct, are those mixtures of hydrocarbons of the paraffin series obtained by purification of the residuum from the distillation of American petroleum. They are recognized in the Pharmacopœia by the names Paraffin, Petrolatum, Liquid Petrolatum, and White Petrolatum. The British and German Pharmacopœias employ only the name Paraffin, but recognize three varieties of the same as hard, liquid, and soft paraffin. Several of these substances are fat-like in appearance and extensively employed as vehicles for the application of numerous remedial agents; commercially they are known as vaseline, cosmoline, albolene, petrolina, etc.

The existence of petroleum in the earth has not as yet been satisfactorily explained; several theories have been advanced, the most acceptable of which is that petroleum is the result of dissociation of large quantities of fatty matter (derived from marine animals), while under long continued pressure, at a moderate temperature, with entire exclusion of air.

American petroleum consists of a mixture of hydrocarbons of the fatty or marsh gas series from methane upward to those richest in carbon, together with small and varying proportions of aromatic

hydrocarbons. Upon subjecting the crude petroleum to a refining process by fractional distillation, benzin or naphtha, illuminating oils, and a residuum largely composed of paraffins are obtained. All fractions are then further purified by treatment with sulphuric acid and subsequently with alkalies, after which they are subjected to further fractional distillation.

Upon distilling the purified residuum from the crude petroleum at higher temperatures, "paraffin oils" are obtained together with a residue of pitch. These paraffin oils are filtered while hot through freshly burned bone-black, for the purpose of removing odor and color, and then subjected to distillation until the desired consistence or melting point of the residuary portion is obtained. The official varieties differ from each other chiefly in the graded removal of lower hydrocarbons.

Paraffins, liquid as well as solid, are not subject to rancidity and if properly purified they consist only of hydrocarbons which are not affected at all by cold acids and alkalies, and only slightly by hot acids; hence the name paraffins has been given to these products from the words *parum*, too little, and *affinis*, allied, on account of their lack of affinity for other substances.

The following are the official varieties of petroleum products more or less extensively used in pharmacy:

Paraffin.—This product, also known as *Hard Paraffin*, is officially defined as a purified mixture of solid hydrocarbons. It is obtained partly as a residue from the distillation of paraffin oils, as stated above, and also largely in Europe by purification with sulphuric acid, etc. of a natural deposit known as *ozokerite* or *crude earth wax*. While insoluble in water and official alcohol, it is freely soluble in ether, petroleum benzin and most warm fixed oils. When entirely free from color, it is often sold under the name paraffin wax, while a yellow variety is known as *ceresin*. Its chief use in pharmacy is in the preparation of paraffin ointment.

Petrolatum, also known as *Petroleum Jelly, Soft Paraffin, Vaseline* and *Cosmoline*.—The Pharmacopœia defines this product as a purified mixture of semisolid hydrocarbons. It is obtained by distilling off the lighter and more volatile portions from the crude petroleum and purifying the residue by treatment with sulphuric acid, sodium hydroxide and animal charcoal. It occurs as an unctuous mass of pale yellow to light amber color, and melts between 38° and 54° C. (100.4° and 129.2° F.). Petrolatum is largely used as a vehicle in the preparation of ointments and as a dressing either alone or medicated.

White Petrolatum, also known as *White Petroleum Jelly* and *White Vaseline*.—This product differs from the preceding only in the more thorough removal of coloring matter, having in other respects all its

characteristic properties. Its use is confined mainly to ointments containing no colored substances, such as ointment of boric acid, etc.

Liquid Petrolatum, also known as *Liquid Paraffin* and *Mineral Oil.*—The Pharmacopœia defines this product as a mixture of liquid hydrocarbons obtained from petroleum. It may be obtained after removal of the lighter hydrocarbons, by subjecting the residuary liquid to distillation between 330° and 390° C. (626° and 734° F.), treating the distillate with sulphuric acid and afterward with caustic soda, and then filtering while hot through animal charcoal, fuller's earth or other decolorizing agent. The liquid is cooled to remove solid paraffin, which will separate, and is then again distilled, the fraction distilling above 330° C. (626° F.) being collected.

The Pharmacopœia recognizes two varieties of liquid petrolatum, designated respectively as Light Liquid Petrolatum and Heavy Liquid Petrolatum, which have many properties in common, but differ in their specific gravities and viscosity. Liquid petrolatum should be colorless and odorless and free from or nearly free from fluorescence; when cold it should be tasteless, and when heated should not develop more than a faint odor of petroleum. The Pharmacopœia requires that liquid petrolatum, when cooled to 10° C. (50° F.) shall not become more than opalescent (limit of solid paraffin).

Since the two varieties of liquid petrolatum are used for different purposes, care should be taken not to confound them; light mineral oil is usually employed as a vehicle for menthol, camphor, thymol, etc., for use as a spray, whereas the heavy mineral oil is used internally as a laxative, The Pharmacopœia requires that the light oil shall have a viscosity not exceeding 3, while the heavy oil shall have a viscosity not below 3.1. This is determined by noting the time in seconds required by equal volumes of distilled water and mineral oil to flow between fixed points marked on a 50 mil. (or Cc.) pipette; then divide the number of seconds required for the flow of mineral oil by the number of seconds required by the distilled water and the quotient will express the viscosity of the oil. The nearer the viscosity of heavy mineral oil comes to 4 the better the quality.

Purified Petroleum Benzin.—Commercial petroleum benzin, usually designated simply as benzin, is a mixture of hydrocarbons, chiefly pentane, C_5H_{12}, and hexane, C_6H_{14}. It is unfit for pharmaceutical purposes unless purified, which is carried out by shaking frequently with an acid solution of potassium permanganate during 24 hours; after decanting the lighter liquid, it is treated for several hours with an alkaline solution of potassium permanganate. Finally it is washed several times with water and again decanted and should then be free from sulphur compounds and other impurities.

Purified petroleum benzin is insoluble in water, but freely soluble in alcohol and miscible with ether, chloroform, benzene and fixed oils

with exception of castor oil, and should distil completely between 40° and 80° C. (104° 176° F.). Its specific gravity varies from 0.638 to 0.660 at 25° C. (77° F.). It is highly inflammable and its vapor, when mixed with air and ignited explodes violently; hence it should be carefully preserved in tin containers or well stoppered bottles in a cool place remote from flame.

Purified petroleum benzin is used in pharmacy for the removal of fatty matter from certain drugs and in the purification of lactucarium and deodorization of opium.

CHAPTER LVIII.

VOLATILE OILS AND RESINS.

VOLATILE oils form a very important class of pharmaceutical plant products. Their physical properties and the mode of obtaining them have already been fully considered on pages 225–235. Chemically, volatile oils differ radically from fats and fixed oils, as they are not capable of saponification and contain no glycerin. Moreover, by exposure to air, they do not become rancid, but many undergo resinification. They may be said to consist of hydrocarbons of the aromatic series, usually associated with oxygen derivatives, alcohols, aldehydes, compound ethers, acids, ketones, and phenols. While some volatile oils are complex mixtures, others are of very simple composition. The hydrocarbons found in volatile oils all belong to one of the following groups: terpenes of the composition $C_{10}H_{16}$, sesquiterpenes of the composition $C_{15}H_{24}$, diterpenes of the composition $C_{20}H_{32}$, and polyterpenes of the composition $(C_{10}H_{16})_x$. The terpenes include dextrorotatory pinene, found in American oil of turpentine; lævorotatory pinene, found in French oil of turpentine; camphene, a solid body, melting at 48°–49° C. (118.4°–120.2° F.), and found in the oils of camphor, citronella, lemon, and others; dextrorotatory limonene (known also as hesperidine, citrene, and carvene), constituting the bulk of the oils of orange peel, lemon, and erigeron, and about 50 per cent. of oil of caraway; lævorotatory limonene, constituting about 50 per cent. of American oil of spearmint; optically inactive limonene, usually designated as dipentene; sylvestrene, found in Swedish and Russian oil of turpentine; phellandrene, of which the dextrorotatory variety is found in oil of water fennel, and the lævorotatory variety forms an objectionable constituent of the oils of eucalyptus; of these pinene and limonene are very widely distributed in nature. Although terpenes frequently form the larger volume of a volatile oil, they may in some instances be considered, from the standpoint of flavor and medicinal properties at least, merely as diluents for the more important constituents, and, on account of their sparing solubility in mixtures of alcohol and water, are frequently removed. Oils thus deprived of their hydrocarbon constituents are known as terpeneless oils, and have been largely offered for sale for a number of years, especially for the manufacture of liquors, essences, and spirits. The group of sesquiterpenes includes cadinene, caryophyllene, cedrene, humulene, and santalene. Other hydrocarbons met with are cymene, myrcene, sabinene, styrene, thujene, etc.

Among the alcohols found in volatile oils, both free and in the form of esters, are allyl, amyl, butyl, methyl and terpin alcohol, borneol, geraniol, linalool, menthol, sabinol, santalol and terpineol. The aldehydes comprise benzoic and cinnamic aldehydes, citral, and citronellal; the ketones, camphor, carvone, and menthone; the phenols and phenolic ethers, carvacrol, chavicol, eugenol, safrol, and thymol. Besides acetic, anisic, benzoic, butyric, formic, salicylic, and valeric acids, sulphocyanic and hydrocyanic acids are also present in some oils; with the exception of hydrocyanic acid they are usually in combination as esters, and but rarely present in the free state.

The behavior of volatile oils with acids, alkalies, and other reagents must naturally vary greatly, owing to the diversity in their constitution. Those oils composed almost wholly of terpenes form either solid or liquid compounds with hydrochloric acid. Other oils are oxidized and converted into resin-like bodies by nitric acid, while sulphuric acid thickens some volatile oils and completely chars others. Color reactions also occur between some of the oils and sulphuric and other acids. Alkali carbonates are without much effect on volatile oils unless the latter contain acids, but alkali hydroxides, in both aqueous and alcoholic solution, are more active, removing phenols, saponifying esters, etc. Acid alkali sulphites, when added to volatile oils containing aldehydes, combine with the latter to form crystalline compounds. Iodine reacts violently with some oils, and bromine forms crystallizable tetrabromides with others.

For the examination of volatile oils both chemical and physical methods are employed; of the former, determination of alcohols, aldehydes, esters, phenols, etc., are important, while of the latter the determination of specific gravity, optical rotation, congealing point, and solubility in alcohol, offers valuable information for deciding upon the true character of the oil.

The specific gravity of volatile oils may be ascertained by means of the Mohr-Westphal balance (see page 61), or a small pycnometer. For the determination of the specific rotation of oils, which is now required in many cases, the necessary explanation may be found on pages 602 and 603 of the Pharmacopœia. The degree of solubility in alcohol is at times useful for detection of certain adulterants, such as oil of turpentine, rectified petroleum, and fatty oils; it is best determined by placing 1 mil. (or Cc.) of the oil in a small cylinder of 10 mils. (or Cc.) capacity, and graduated into $\frac{1}{2}$'s or $\frac{1}{10}$'s, and adding small portions of 90, 80, or 70 per cent. alcohol, as the test may require, until, after vigorous agitation, a perfectly clear solution results, free from turbidity and separation. As determination of the congealing point is required for only two of the official oils, the method will be given under the respective oils.

The following analytical methods in use among chemists give an idea as to the mode of determining quantitatively some of the chief constituents of volatile oils.

Determination of esters, such as are found in the oils of bergamot, lavender, orange flowers, peppermint, and wintergreen: Place about 2 Gms. of the oil, accurately weighed, into a suitable 100 mil. (or Cc.) flask provided with a sound cork and a reflux condenser; in place of the condenser, a glass tube thirty-six or forty inches long may be used. Add 20 mils. (or Cc.) of half-normal alcoholic potassium hydroxide solution to the oil and heat the mixture to boiling on a waterbath for one hour. When cool dilute the contents of the flask with about 50 mils. (or Cc.) of distilled water and titrate the excess of alkali by means of half-normal sulphuric acid. From the number of mils. (or Cc.) of half-normal potassium hydroxide solution thus ascertained as having been required for saponification of the ester in the oil calculate the number of milligrams of potassium hydroxide required (1 mil. (or Cc.) $\frac{N}{2}$ KOH sol. = 0.028055 Gm. KOH) for 1 Gm. of the oil, and from this find the percentage of ester originally present. Every milligram of KOH required for 1 Gm. of the oil represents 0.348 per cent. of acetate of alcohols of the composition $C_{10}H_{17}OH$, or 0.351 per cent. of acetate of alcohols of the composition $C_{10}H_{19}OH$, as shown by the following proportions:

$$\begin{array}{llllll} \text{KOH} & C_{10}H_{17}C_2H_3O_2 & \text{KOH} & C_{10}H_{17}C_2H_3O_2 & \\ 56.11 : & 195.152 & :: 0.001 : & x & x = 0.003478 +. \end{array}$$

$$\begin{array}{llllll} \text{KOH} & C_{10}H_{19}C_2H_3O_2 & \text{KOH} & C_{10}H_{19}C_2H_3O_2 & \\ 56.11 : & 197.168 & :: 0.001 : & x & x = 0.003513 +. \end{array}$$

The figures in the above calculations refer to the presence of esters as acetates only; when benzoates, salicylates, or other esters are present, or a possible mixture of these with acetate, the results may be reported either as equivalent to so much acetate or different calculations made for other esters if they alone be present.

Determination of alcohols: Since the different alcohols met with in volatile oils are rarely, if ever, present wholly in an uncombined state, it becomes necessary to determine, first, the amount in combination as esters and then the total amount present, and, lastly, find the amount of uncombined alcohol by difference. Having saponified a given weight of the oil by the method above explained, the percentage of alcohol present as an ester can be readily calculated by multiplying the number of mils. (or Cc.) of half-normal potassium hydroxide solution required for saponification by 0.077072 for alcohols having the composition $C_{10}H_{17}OH$, or by 0.07808 for alcohols belonging to the $C_{10}H_{19}OH$ group, then dividing the product by the weight of oil used and multiplying the quotient by 100. The next step is to convert the uncombined alcohol into an ester, which is done by acetylization. Into a suitable flask, provided with a reflux condenser ground into the neck, as shown in Fig. 336, are put 10 Gms. of the oil, an equal volume of acetic anhydride $(C_2H_3O)_2O$, and 1 Gm. of anhydrous sodium acetate; the mixture is then boiled for an hour and cooled. The product is transferred to a separator, and washed well with

water, then with a dilute solution of sodium carbonate, and, again with water until the reaction is neutral, and is finally dried with anhydrous calcium chloride or sodium sulphate. About 2 Gms., accurately weighed, of the dry acetylized oil are transferred to a suitable flask, using a small quantity of 95 per cent. ethyl alcohol to transfer the last portions, and saponified with 20 mils. (or Cc.) of normal alcoholic potassium hydroxide solution in the manner explained in the preceding paragraph, except that normal sulphuric acid must be used in this case to titrate the excess of alkali. If the number of mils. (or Cc.) of normal alkali required by the oil be now multiplied by 0.154144 or 0.15616 the total amount of alcohol present

FIG. 336.—Acetylization flask.

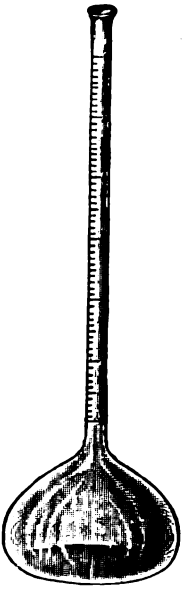


FIG. 337.—Aldehyde flask.

in the oil taken will be found, and this multiplied by 100 and then divided by the weight of acetylized oil used for the assay, will give the percentage. The difference between this percentage and that of alcohol found in combination represents the uncombined alcohol.

The method is well adapted for the quantitative determination of borneol, geraniol, and menthol, but does not give satisfactory results with linalool and terpineol. If aldehydes are also present in the oil the acetylization method cannot be used.

Determination of aldehydes: The well known property of aldehydes of forming water-soluble addition-compounds with acid sodium sulphite is made use of in determining the aldehyde content of volatile oils quantitatively. Cinnamic aldehyde in oil of cassia cinnamon,

and citral in oil of lemongrass, can both be determined very satisfactorily by the following method, which is based on the observation that when either oil is shaken for some time with hot acid sodium sulphite solution the decrease in volume of the oil corresponds about to the proportion of aldehyde present. For this purpose use is made of a special flask of about 100 mil. (or Cc.) capacity with a long, narrow neck (13 x .8 cm.), which is graduated into tenths of a mil. (or Cc.). (See Fig. 337.) Exactly 10 mils. (or Cc.) of the oil are put into the flask by means of a pipette, and a like volume of a warm 30 per cent. solution of acid sodium sulphite is added. The flask is placed in a boiling waterbath, and more of the acid sulphite solution is gradually added until a uniform fluid is obtained, filling the flask nearly three-fourths. When all solid particles, at first formed, have disappeared and the characteristic odor of the respective aldehyde is no longer discernible, the flask is filled with acid sulphite solution up to the zero point of the graduated scale. The uncombined oil rises in the neck of the flask, and its volume may be accurately red off and subtracted from 10, from which the volume percentage of aldehyde is easily calculated. Oil of cassia, of good quality, contains from 70–90 per cent. of its characteristic aldehyde, and oil of lemongrass from 60–85 per cent. The above method cannot be employed for oils containing only small proportions of aldehyde, as oil of lemon, which contains 4–10 per cent. of citral.

Determination of phenols: Advantage may be taken of the solubility of nearly all phenols in solutions of caustic alkali to determine the amount present in volatile oils, from the diminution of volume which the oil suffers when thus treated. It is the official method of assay directed for oil of clove and oil of thyme, but as a small portion of the non-phenolic part of the oil is liable to be lost during the operation, being carried into solution along with the phenol, the results will be slightly high.

For the determination of thymol and carvacrol the following somewhat more tedious method will yield more accurate results; it is not suitable, however, for the determination of eugenol in oil of clove: From a weighed flask of oil about 5 mils. (or Cc.) are poured into a glass stoppered burette graduated to $\frac{1}{10}$ mil. (or Cc.). By again weighing the flask of oil the weight of the sample taken is found by difference. Add an equal volume of petroleum ether to the oil in the burette and mix well. Now add some 5 per cent. potassium hydroxide solution and shake vigorously for some time; allow the liquids to separate perfectly and allow the alkaline solution to run into a 100 mil. (or Cc.) graduated flask. This treatment with alkali is repeated several times until no further decrease in the volume of the oil is observed and all phenol has been abstracted. The solution of phenols is then made up to 100 mils. (or Cc.) by addition of 5 per cent. potassium hydroxide solution, and 10 mils. (or Cc.) of this dilution put into a 500 mil. (or Cc.) flask. A known quantity of tenth-

normal iodine solution is now added, by which thymol is precipitated as a dark, reddish-brown compound, but carvacrol as one of milky appearance. A large excess of iodine is not desirable, and a few drops of the liquid put into a tube containing diluted hydrochloric acid and showing an iodine color indicates a sufficiency. In the case of thymol the solution in the flask is now made slightly acid with dilute hydrochloric acid and diluted to 500 mils. (or Cc.) by addition of water. From this 100 mils. (or Cc.) are filtered off and the excess of iodine titrated with tenth-normal sodium thiosulphate solution.

The number of mils. (or Cc.) required multiplied by 5 and deducted from the number of mils. (or Cc.) of tenth-normal iodine solution originally added to the alkaline solution gives the number of mils. (or Cc.) of iodine solution required by the phenol.

The reaction involved in this method is expressed by the following equation: $C_{10}H_{14}O + I_4 + 2NaOH = C_{10}H_{12}I_2O + 2NaI + 2H_2O$, from which it is seen that each molecule of thymol requires 4 atoms of iodine in the presence of sodium hydroxide, and hence each mil. (or Cc.) of tenth-normal solution used in the reaction with thymol or carvacrol will correspond to 0.0037528 Gm. of the phenol. This factor, multiplied by the number of mils. (or Cc.) of the iodine solution used, and then by 100, and divided by the weight of the oil originally put into the burette, will express the percentage of phenol in the oil.

For oils containing carvacrol a slight modification of the method is necessary. After addition of the iodine solution the milky liquid must be actively shaken, in order that the precipitate may become flocculent and the solution clear or nearly so. The mixture is now diluted to 500 mils. (or Cc.) by addition of water and 100 mils. (or Cc.) filtered off. The filtrate is slightly acidulated with hydrochloric acid and the excess of iodine titrated with tenth-normal sodium thiosulphate solution. The calculations are the same as in the case of thymol.

THE OFFICIAL VOLATILE OILS.

Oil of Anise.—The chief constituent of this oil, 90 per cent. and over, is anethol, $C_6H_4C_3H_5OCH_3$, which solidifies at low temperatures and is accompanied by an isomeric liquid body known as methylchavicol.

Under the official name, both the oil of common anise and that of star anise are recognized, the fruit alone, however, being designated as the source, thus excluding oil of anise leaves. The Pharmacopœia requires that the botanical source of the oil shall be stated on the label. The two oils differ but slightly in chemical and physical properties, and, commercially as well as pharmaceutically, distinction between the two is rarely practised. The German Pharmacopœia applies the Latin title Oleum Anisi also to anethol, the chief constituent of oil of anise, and describes it as a white crystalline mass congealing between 15° and 19° C. (59° and 66.2° F.).

Oil of anise is lævogyrate, deflecting the ray of polarized light 2 degrees to the left in a 100 mm. tube at 25° C. (77° F.), and in this way may be distinguished from oil of fennel, which latter likewise contains considerable anethol, but is dextrogyrate to the extent of from 12 to 24 degrees. The Pharmacopœia requires that, when tested by the following method, the congealing point of oil of anise shall not be below 15° C. (59° F.): Transfer about 10 mils. (or Cc.) of the oil to a test tube, placed in water cooled with ice; insert a thermometer at once into the oil, and allow it to remain undisturbed until its temperature has fallen to about 12° C. (53.6° F.). Induce crystallization either by scratching the inner wall of the test tube with the thermometer, or by the addition of a particle of solid anethol, remove the test tube from the bath, and stir continuously during the solidification of the oil. The highest temperature reached during the crystallization is regarded as the congealing point.

Oil of Betula.—This oil, also known as oil of sweet birch, is no longer official under its former title, see Methyl Salicylate, p. 789. Investigations made by Power and Kleber (1895) have shown that oil of sweet birch, in its unrectified state, contains about 99.8 per cent. of methyl salicylate, together with a very small amount of a paraffin triacontan, $C_{30}H_{62}$, an aldehyde or ketone, and the ester, $C_{14}H_{24}O_2$; it does not, however, contain the alcohol $C_8H_{16}O$, found in oil of gaultheria.

Empyreumatic oil of birch, known commercially as *oleum rusci* and also as *oleum betulinum* or *oleum muscoviticum*, is obtained by distillation of birch tar or *daggett*, derived by destructive distillation from the wood of the common European birch, betula alba. The oil is of a dark, brown-red color, having a peculiar penetrating odor like that of Russian leather, and somewhat resembles oil of cade in its medicinal properties.

Oil of Bitter Almond.—The oil to which this name is applied need not necessarily be obtained from bitter almonds, the Pharmacopœia recognizing also the volatile oil produced from other seeds containing the glucoside amygdalin, provided the botanical source of the oil is stated on the label of the container and the oil conforms to the official requirements of not less than 85 per cent. of benzaldehyde, and not less than 2, nor more than 4, per cent. of hydrocyanic acid. The oil does not pre-exist in the seed, but is produced from amygdalin by fermentation set up in the presence of water, as shown by the equation $C_{20}H_{27}NO_{11}$ (amygdalin) + $2H_2O$ = C_6H_5COH (benzoic aldehyde or benzaldehyde) + HCN (hydrocyanic acid) + $2C_6H_{12}O_6$ (dextrose). Previous to the distillation of the volatile oil, the seeds must be deprived of their fatty oil by powerful pressure applied to the crushed seed, the presscake being subsequently ground to fine powder and mixed with 6 or 8 parts of warm water, not above 50°

or 60° C. (122°–140° F.), and allowed to stand for about twelve hours so that the reaction may be completed, after which the oil formed is distilled with steam by passing the same through the mixture.

Oil of bitter almond is optically inactive or only very slightly dextrorotatory. It is soluble in about 300 parts of water and in twice its volume of 70 per cent. alcohol.

Exposed to the air, oil of bitter almond slowly undergoes oxidation, especially in half-filled bottles, the benzoic aldehyde being converted into benzoic acid, C_6H_5COOH. Crystals of the acid are sometimes seen in old oil, and when thus contaminated the oil should not be used.

The Pharmacopœia directs that the determination of the benzaldehyde content be made by means of an alcoholic solution of freshly distilled phenylhydrazine, the value of which is first ascertained by titration with half-normal hydrochloric acid; the hydrocyanic acid content is determined in the usual manner with tenth-normal silver nitrate solution.

The first assay, for benzaldehyde, depends upon the reaction between phenylhydrazine, $C_6H_5NH.NH_2$, and the benzaldehyde in the oil, C_6H_5COH, resulting in the formation of crystallizable benzalphenylhydrazone and water, thus: $C_6H_5NH.NH_2 + C_6H_5COH = C_6H_5CH.N.NHC_6H_5 + H_2O$. As half-normal hydrochloric acid is used to titrate the excess of phenylhydrazine, each mil. (or Cc.) of the difference between the amount required and the amount used for titration of an equal volume of the original phenylhydrazine solution must correspond to $\frac{1}{1000}$ of one-half of the molecular weight of benzaldehyde expressed in grams, or 0.053 Gm. ($106.048 \div 2 \div 1000 = 0.053024$). The number of mils. (or Cc.) representing the difference, therefore, when multiplied by 5.3 (0.053×100) and divided by the weight of oil of bitter almond taken for the assay, will express the percentage of benzaldehyde present in the oil.

In the assay for hydrocyanic acid, the first step results in the precipitation of magnesium hydroxide, which forms a better background for observation of the red color of the newly formed silver chromate. Upon addition of oil of bitter almond, the hydrocyanic acid present discharges this color, which then is reproduced after all hydrocyanic acid has been precipitated by the silver nitrate solution as silver cyanide. As 1 molecule of silver nitrate is capable of precipitating 1 molecule of hydrocyanic acid, thus, $AgNO_3 + HCN = AgCN + HNO_3$, each mil. (or Cc.) of tenth-normal silver nitrate solution must correspond to 0.0027 Gm. of hydrocyanic acid. The number of mils. (or Cc.) of the silver nitrate solution required for reappearance of the red color, therefore, when multiplied by 0.27 (0.0027×100) and divided by the weight of oil of bitter almond taken for the assay, will express the percentage of hydrocyanic acid present in the oil.

Considerable synthetic oil of bitter almond is offered for sale, which is made from toluene, and is recognized in the Pharmacopœia

as Benzaldehyde. This contains no hydrocyanic acid, but, if imperfectly purified, may contain chlorinated by-products, and hence the Pharmacopœia gives special tests to indicate their absence in oil of bitter almond. The presence of other volatile oils may be ascertained by treatment with acid sodium sulphite solution, whereby an addition compound of benzaldehyde is formed, $C_6H_5COH.NaHSO_3$, which goes into solution upon application of heat, and may thus be removed, leaving other oils floating on the surface.

Oil of Cade.—This oil, obtained by destructive distillation of the wood of the prickly cedar, a species of juniper indigenous to the southern part of France, is also known as *oil of juniper tar* and *empyreumatic oil of juniper*, and consists of a sesquiterpene, cadinene, $C_{15}H_{24}$, and a mixture of undetermined phenols.

Cade oil is practically insoluble in water, but imparts to it an acid reaction; it is partially soluble in alcohol and in petroleum benzin and wholly soluble in ether and in oil of turpentine. Among the possible adulterations of cade oil are rosin and rosin oil, which can be detected by means of copper acetate solution as directed in the Pharmacopœia.

Oil of Cajuput.—The constituents are a neutral body, cineol or eucalyptol, $C_{10}H_{18}O$ (about 67 per cent.), an alcohol, terpineol, $C_{10}H_{17}OH$, some pinene and undetermined terpenes.

Although the chief constituent of oil of cajuput is optically inactive, the oil is slightly lævogyrate, to the extent of about 4 degrees, owing to the invariable presence of lævorotatory pinene.

The Pharmacopœia no longer demands a definite percentage content of cineol, but the British Pharmacopœia requires the presence of not less than 45 per cent., to be determined as cineol phosphate in the manner formerly official in our own Pharmacopœia.

Oil of Caraway.—This oil is composed of a terpene, limonene, $C_{10}H_{16}$ and a ketone, carvone, $C_{10}H_{14}O$, formerly known as carvol; both compounds are dextrorotatory and are present in proportions varying from 35 to 50 of the former to 65 to 50 of the latter.

Carvone is the important constituent of oil of caraway. The angle of rotation of the oil varies from +70° to +80°, and since it is +62.5° for pure carvone and +125° for pure limonene, it is evident that the rotatory power of the oil will increase with a diminished carvone content. The Pharmacopœia requires that oil of caraway shall contain not less than 50 per cent. of carvone, to be determined volumetrically by shaking a definite volume of the oil with sodium sulphite solution in a graduated flask (see p. 770) and noting the decrease in volume of the oil, which represents the carvone present, since the terpene limonene is not soluble in the sulphite solution.

Oil of Chenopodium.—Until recently little was known as to the composition of oil of American wormseed. By fractional distillation at reduced pressure a yellow oily liquid of peculiar repulsive odor was obtained by Schimmel & Co. in 1908, and by E. K. Nelson in this country in 1910 and 1913, to which the name ascaridole has been given; it constitutes about 70 per cent. of the oil of chenopodium and on analysis afforded the formula $C_{10}H_{16}O_2$. Ascaridole has been found absolutely indifferent toward reagents which would characterize it as an aldehyde, ketone, phenol or alcohol.

Nearly all oil of chenopodium obtained in this country is distilled in Maryland and is usually marketed as Baltimore oil of wormseed. It is soluble in 8 volumes of 70 per cent. alcohol and its optical rotation varies from $-4°$ to $-10°$ in a 100 mm. tube at 25° C.

Oil of Cinnamon.—Ordinary oil of Chinese cinnamon, usually designated as *oil of cassia*, is the kind recognized in the U. S. Pharmacopœia, whereas the British and German Pharmacopœias recognize the oil of Ceylon cinnamon. It consists chiefly of cinnamic aldehyde, C_8H_7COH, with some cinnamyl acetate, $C_9H_9C_2H_3O_2$, and small amounts of cinnamic acid, $C_9H_8O_2$, or $C_6H_5CHCHCOOH$. The value of this oil, which has been subject to adulteration, depends upon the amount of cinnamic aldehyde present, of which it should contain not less than 80 per cent. by volume, and which may be determined with acid sodium sulphite, as explained on page 770. The chemical reactions involved in the official assay process may be shown by the following equations, an insoluble aldehyde addition compound being first formed, to which the name sodium cinnamalhydroxysulphonate has been given; this when boiled with water breaks up into cinnamic aldehyde and sodium sulphocinnamalhydroxysulphonate, thus: $C_8H_7COH + NaHSO_3 = C_8H_7COH.NaHSO_3$; $2C_8H_7COH.NaHSO_3 = C_8H_7COH + C_6H_5CH_2CH(SO_3Na).COH.NaHSO_3$. In order to convert all of the aldehyde present into the second compound soluble in water, an excess of acid sodium sulphite must be added.

Oil of Ceylon cinnamon, which has a finer aroma than the official oil contains, besides cinnamic aldehyde, some eugenol and phellandrene.

Oil of Clove.—The chief constituent of this oil is eugenol, $C_6H_3.C_3H_5.OCH_3.OH$, a monatomic phenol, which is present in prime oil to the extent of from 75 to 85 per cent. and over; besides this, the oil also contains a sesquiterpene, $C_{15}H_{24}$, called caryophyllene, and about 2 or 3 per cent. of eugenol acetate.

The value of oil of clove lies wholly in the eugenol present, of which the Pharmacopœia requires not less than 82 per cent. to be present. The simplest method for determining the eugenol content of oil of clove is that of shaking 10 mils. (or Cc.) of the oil with 50 mils (or Cc.) of official potassium hydroxide solution for five minutes in a

suitably graduated flask (see Fig. 334, p. 770); then heat on a water-bath during ten minutes, cool and allow the liquids to separate, adding sufficient alkali solution to raise the lower limit of the oily layer to the zero point of the graduated scale, and note the volume of oil remaining, which substracted from 10 indicates the number of mils. (or Cc.) of eugenol dissolved by the alkali solution, and multiply the remainder by 10 to find the percentage of phenol in the sample of oil. This method, while easily applied, is not absolutely accurate, as already explained on page 771, but should always be used when an oil appears at all suspicious, in view of the fact that oil of clove is sometimes met with from which a portion of the eugenol has been abstracted. A more accurate determination of eugenol in oil of clove is to convert it into crystalline benzoyl eugenol, $C_{10}H_{11}OC_6H_5CO$, by means of benzoyl chloride, and to calculate from the weight of the crystalline compound formed the percentage of eugenol in the oil. The method is given in the *American Journal of Pharmacy* for 1892, page 508.

Oil of Coriander.—The oil consists of about 90 per cent. of linalool and about 6 per cent. of pinene, together with some unknown substance, to which the peculiar aroma is due. It is soluble in 3 volumes of 70 per cent. alcohol and in all proportions of 80 and 90 per cent. alcohol. Oil of coriander is dextrogyrate, its angle of rotation varying from 8° to 13° in a 100 mm. tube at 25° C. (77° F.)

Oil of Cubeb.—The composition of this oil varies somewhat with age. Recent oil, distilled from fresh fruit, consists chiefly of a sesquiterpene, cadinene, $C_{15}H_{24}$, with some dipentene, $C_{10}H_{16}$, but if old or obtained from old fruit, cubeb camphor, $C_{15}H_{24}.H_2O$, is also present. The oil is lævogyrate, the angle of rotation varying from −20° to −40° in a 100 mm. tube at 25° C.

Oil of Eucalyptus.—The composition of this oil depends largely on its source. The oils of Eucalyptus globulus and Eucalyptus oleosa consist chiefly of cineol, which in the case of eucalyptus oils is generally called eucalyptol and to which they owe their medicinal and antiseptic value; the former oil contains also some pinene and a ketone, $C_{10}H_{16}O$, called eudesmol, while the latter oil, in place of eudesmol contains a sesquiterpene and an aldehyde, $C_{10}H_{13}COH$, known as aromadendral and resembling cumin aldehyde in odor. The less valuable oils of eucalyptus contain less cineol, but pinene and varying amounts of phellandrene. The test for the presence of excessive quantities of phellandrene in oil of eucalyptus depends upon the formation of crystalline phellandrene nitrite and can be made more delicate, according to Power, by mixing the oil first with 5 mils. (or Cc.) of petroleum benzin, then adding the sodium nitrite solution and lastly the glacial acetic acid, drop by drop.

The Pharmacopœia demands that oil of eucalyptus shall contain

not less than 70 per cent. by volume of eucalyptol, which is determined by conversion into eucalyptol arsenate, as directed in the official assay method; the crystalline mass having been well washed and dried is transferred to a graduated cassia flask, decomposed by means of hot water and the volume of eucalyptol liberated is allowed to rise in the graduated neck of the flask and cool. If 10 mils. (or Cc.) of the oil are used for the assay, the volume of eucalyptol collected in the neck of the flask, when multiplied by 10, will express the exact percentage present in the sample of the oil.

Oil of eucalyptus is somewhat dextrogyrate, but the angle of rotation should not be greater than 10°, eucalyptol being inactive optically; the greater the eucalyptol content the lower the angle of rotation.

Some eucalyptus oils contain also citral, $C_{10}H_{16}O$, citronellal, $C_{10}H_{18}O$, and geraniol, $C_{10}H_{17}OH$.

Oil of Fennel.—This oil contains the terpenes, pinene, phellandrene, and dipentene, together with fenchone, $C_{10}H_{16}O$, and anethol, $C_{10}H_{12}O$; the latter is usually present to the extent of more than 50 per cent. and separates in crystals upon a reduction of the temperature, hence the higher the temperature at which this occurs the better the oil. The Pharmacopœia has fixed the congealing point at not below 3° C. (37.4° F.) to be determined as follows: Transfer about 10 mils. (or Cc.) of the oil to a test tube placed in a freezing mixture; insert a thermometer at once into the oil, and allow it to remain undisturbed until the temperature has fallen to 0° C. (32° F.). Induce crystallization either by scratching the inner wall of the test tube with the thermometer or by the addition of a particle of solid anethol, and stir continuously during the solidification of the oil. The highest temperature reached during the crystallization is regarded as the congealing point.

Oil of fennel is dextrogyrate, its angle of rotation varying from 12° to 24°, which, together with the higher congealing point of oil of anise, readily distinguishes the two oils from each other.

Oil of Gaultheria.—This oil, also known as oil of wintergreen, is, as in the case of oil of betula, no longer official under its former title, see Methyl Salicylate, p. 789. The true oil contains, according to Power and Kleber, 1895, about 99 per cent. of methyl salicylate together with a small amount of paraffin, probably triacontan, $C_{30}H_{62}$, an aldehyde or ketone, an apparently secondary alcohol, $C_8H_{16}O$, and an ester, $C_{14}H_{24}O_2$, formed by this alcohol and an acid, $C_6H_{10}O_2$, which latter is the result of oxidation of the aldehyde previously mentioned. The alcohol and the ester are said to possess the very penetrating odor characteristic of true oil of gaultheria.

Oil of Juniper.—The chief constituent is pinene, with some cadimene, $C_{15}H_{24}$, and a body, as yet undetermined, to which the peculiar

odor and taste of the oil are due. The oil obtained from the fruit only should be used in pharmacy, and it would seem best to designate it always as oil of juniper berries.

Oil of Lavender.—Two varieties of this oil, English and French, are found on the market, the former being usually designated as oil of garden lavender, because distilled from cultivated plants. The French oil of lavender is no doubt always sent on orders when simply oil of lavender is mentioned, on account of lower price. The Pharmacopœia makes no distinction between the two oils and in not demanding a definite ester content recognizes any oil of lavender that meets the other official requirements. The British Pharmacopœia demands from 7 to 11 per cent. of linalyl acetate for English oil and not less than 30 per cent. of the ester for foreign oils. Both oils are lævogyrate, the angle of rotation not exceeding $-10°$, and form clear solutions with 3 parts of 70 per cent. alcohol.

The percentage of ester, linalyl acetate, present in any sample of oil of lavender may be determined by the general method of saponification with alcoholic solution of potassium hydroxide, as explained on page 769.

Oil of Lemon.—Quantitatively, the chief constituent of oil of lemon is dextrorotatory limonene, but an aldehyde known as citral, $C_9H_{15}COH$, is of much greater importance, although rarely present to the extent of more than 6 or 8 per cent. Other constituents of the oil are pinene, phellandrene, citronellal, geranyl acetate, etc. The most dangerous adulteration of oil of lemon is perhaps the residue or by-product obtained in the manufacture of terpeneless oil of lemon, and hence an assay of the citral content should be made whenever suspicion is aroused in connection with any sample of the oil. The Pharmacopœia demands the presence of not less than 4 per cent. of aldehydes calculated as citral, to be determined in a manner practically identical with the assay of benzaldehyde in oil of bitter almond, which see, on page 774.

The reaction occurring between citral and phenylhydrazine is very similar to that taking place when benzaldehyde and phenylhydrazine are brought together, citralphenylhydrazone being formed, thus $C_9H_{15}COH + C_6H_5NH.NH_2 = C_9H_{15}CH.N.NHC_6H_5 + H_2O$. The excess of phenylhydrazine being determined by titration with halfnormal hydrochloric acid, each mil. (or Cc.) of the difference between the amount of the acid required and the amount used in a blank test for titration of a volume of phenylhydrazine solution equal to that originally added to the oil of lemon, must correspond to $\frac{1}{1000}$ of $\frac{1}{2}$ of the molecular weight of citral expressed in grams, or 0.0761 Gm. ($152.13 \div 2 \div 1000 = 0.076065$). The number of mils. (or Cc.) of half-normal acid representing the difference, therefore, when multiplied by 7.61 (0.0761×100) and divided by the weight of oil of lemon taken for the

assay, will express the percentage of aldehydes, calculated as citral, present in the oil.

Oil of Mustard, Volatile.—Like oil of bitter almond, this oil does not pre-exist in the plant; it is obtained by macerating crushed black mustard seed, after the removal of fixed oil by expression, with water, when a reaction sets in between sinigrin, a glucoside, and myrosin, an albuminoid body. Sinigrin is, chemically, potassium myronate, $C_{10}H_{18}NS_2KO_{10}$, which, under the influence of the albuminoid ferment, is split up into allyl isosulphocyanate, acid potassium sulphate, and dextrose, thus: $C_{10}H_{18}NS_2KO_{10} = C_3H_5NCS$ (volatile oil of mustard) + $KHSO_4$ + $C_6H_{12}O_6$. Since the albuminoid myrosin is rendered inert at a temperature between 60° and 70° C. (140° and 158° F.), mustard which has been heated to this point will not yield the volatile oil, nor can hot water be employed in its manufacture; for the same reason, mustard plasters should never be dipped into water that is more than lukewarm.

White mustard seed does not yield volatile oil of mustard, since it does not contain sinigrin, but, instead, sinalbin, having the composition $C_{30}H_{44}N_2S_2O_{16}$. When sinalbin reacts with myrosin in the presence of water, a very active, oily but non-volatile principle, to which the name acrinyl sulphocyanate, $C_7H_7O.CSN$, has been given, is formed, together with acid sinapine sulphate, $(C_{16}H_{23}NO_5)H_2SO_4$, and glucose, $C_6H_{12}O_6$.

The official method of valuation depends upon the formation of thiosinamine by the action of ammonia on allyl isosulphocyanate, thus, $C_3H_5NCS + NH_3 = C_3H_5CSN_2H_3$; this is acted upon by the silver nitrate, or rather silver in the form of oxide held in solution by the ammonia, whereby the sulphur is removed and a new compound, allylcyanamide, $CN.NH.C_3H_5$, is produced, thus, $C_3H_5CSN_2H_3 + Ag_2O = Ag_2S + CN.NH.C_3H_5 + H_2O$. As each molecule of thiosinamine, representing 1 molecule or 99.12 parts of allyl isosulphocyanate, requires 1 molecule of silver oxide obtained from 2 molecules or 339.78 parts of silver nitrate for complete removal of the sulphur present, each mil. (or Cc.) of the silver solution containing 0.016989 Gm. of silver nitrate corresponds to 0.004956 Gm. of allyl isosulphocyanate; the excess of silver solution is determined by titration with potassium sulphocyanate solution. As the Pharmacopœia requires that volatile oil of mustard shall yield not less than 92 per cent. of allyl isosulphocyanate, each 0.1 Gm. of the oil will require not less than 18.56 mils. (or Cc.) of tenth-normal silver nitrate solution, for 92 per cent. of 0.1 is 0.092 and 0.092 divided by 0.004956 = 18.563.

Volatile oil of mustard is largely made synthetically by decomposing allyl iodide, C_3H_5I, by means of potassium sulphocyante in alcoholic solution, and the Pharmacopœia requires that the oil shall be labeled to show whether it has been made synthetically or obtained from black mustard seed.

Oil of Nutmeg.—The Pharmacopœia recognizes only the volatile oil obtained from the kernel of the ripe seed of nutmeg as oil of myristica, whereas in Germany the oil distilled from mace, the arillus of the nutmeg, is officially named as ethereal oil of nutmeg. The two oils resemble each other closely in physical properties and chemical composition, although the oil obtained from the seed contains a larger proportion of terpenes than oil of mace, and is more decidedly dextrogyrate, its angle of rotation ranging from 12° to 30° in a 100 mm. tube at 25° C. (77° F.). The chemical constituents of both oils are pinene, dipentene, myristicol $C_{10}H_{16}O$, myristicin $C_{12}H_{14}O_3$, and some myristinic acid.

The expressed or fatty oil of nutmeg, containing about 6 per cent. of volatile oil, is recognized in the German Pharmacopœia as Oleum Nucistæ, although the official German title is oil of nutmeg. It is better known as nutmeg butter.

Oil of Orange.—The official oil of orange is that obtained by expression only from the fresh rind of the sweet orange, since some of the constituents upon which the odor of the oil depends are destroyed in part by distillation. Oil of orange contains about 90 per cent. of dextrorotatory limonene, together with the aldehydes citral and citronellal, and some methyl anthranilate, $CH_3C_9H_6NO_2$. It is strongly dextrogyrate, showing a rotation of not less than 94° in a 100 mm. tube at 25° C. (77° F.). The refractive index of oil of orange is given as 1.4723 to 1.4737 at 20° C. (68° F.) and the Pharmacopœia requires that if 5 mils. (or Cc.) of distillate be obtained from 50 mils. (or Cc.) of the oil in a Ladenburg flask of specified dimensions, at the rate of 1 drop per second, the refractive index of this distillate at 20° C. (68° F.) shall not be less than 0.0008 nor more than 0.0015 lower than that of the original oil, and also that the optical rotation of the distillate shall be equal to or only slightly greater than that of the original oil.

Oil of orange, like oil of lemon, when carelessly exposed to air and light, gradually assumes a terebinthinate odor, which can be prevented by addition of 5 or 10 per cent. of pure alcohol.

Oil of bitter orange, also offered for sale, closely resembles that obtained from the sweet orange, but is not officially recognized.

Oil of Peppermint.—There is probably no volatile oil used in pharmacy of which a greater variety is offered for sale; besides five or six different brands of American oil, oils distilled from English, German, and Japanese peppermint herb are also on the market. Oil of peppermint shows a greater complexity in composition than any other volatile oil known, an analysis in 1894 by Power and Kleber of the average American oil having developed the following constituents, fifteen in number: Acetaldehyde, C_2H_4O; acetic acid, $HC_2H_3O_2$; iso-valeraldehyde, $C_5H_{10}O$; iso-valeric acid, $HC_5H_{10}O_2$; three iso-

meric terpenes, pinene, phellandrene, and limonene, $C_{10}H_{16}$; cineol or eucalyptol, $C_{10}H_{18}O$; menthone—a ketone—$C_{10}H_{18}O$; menthol, $C_{10}H_{19}OH$; two compound ethers, menthyl acetate, $C_{10}H_{19}C_2H_3O_2$, and menthyl iso-valerate, $C_{10}H_{19}C_5H_{10}O_2$; a sesquiterpene, cadinene, $C_{15}H_{24}$; and a lactone of the composition $C_{10}H_{16}O_2$.

The most important constituent is menthol. The Pharmacopœia requires that oil of peppermint shall contain not less than 5 per cent. of esters, calculated as menthyl acetate, and not less than 50 per cent. of total menthol (free and combined), both of which may be determined according to the general directions given for the estimation of alcohols and esters on page 769. As 1 molecule or 198.18 parts of menthyl acetate requires 1 molecule of potassium hydroxide, as shown by the equation $C_{10}H_{19}C_2H_3O_2 + KOH = C_{10}H_{19}OH + KC_2H_3O_2$, for complete saponification, each mil. (or Cc.) of half-normal alcoholic potassium hydroxide solution, containing 0.028055 KOH, corresponds to 0.09909 Gm. of menthyl acetate; hence in the official test the number of mils. (or Cc.) of half-normal alkali solution required must be multiplied by 9.909 (0.09909×100) and the product divided by the weight of oil taken, to obtain the percentage of esters present.

For determination of the total menthol, the Pharmacopœia directs that the oil be acetylized by boiling it with acetic anhydride and anhydrous sodium acetate for one hour in a special flask, see Fig. 336 on page 770, the acetylized oil being then thoroughly washed with water and a weak solution of sodium carbonate and finally dried with the aid of fused calcium chloride. The product of this treatment now contains not only the menthyl acetate that was present in the original oil before acetylization, but also the menthyl acetate which results from the menthol that was free or uncombined in the oil before acetylization. In this dried acetylized oil the total menthol is then determined by saponification of the ester, menthyl acetate, with half-normal alcoholic potassium hydroxide solution.

The figure obtained by using the formula for calculation given in the Pharmacopœia, which is called the percentage of total menthol in the oil of peppermint, is in reality not such, but is the percentage of total menthol in the oil as it would be if there were no menthyl acetate in it originally, but only uncombined menthol. This is arbitrarily called the percentage of total menthol and is only slightly larger than the figure that would be obtained if the calculation were made on the original oil of peppermint, and is more easily calculated. The formula in the Pharmacopœia is

$$\text{Percentage of menthol} = \frac{A \times 7.808}{B - (A \times 0.021)}$$

in which A represents the number of mils. (or Cc.) of half-normal alcoholic potassium hydroxide solution required for saponification of the ester in the acetylized oil taken for the assay, or in other words the

result obtained by subtracting the number of mils. (or Cc.) of half-normal sulphuric acid required in the titration, from the number of mils. (or Cc.) of half-normal alcoholic potassium hydroxide solution originally added; the figure 7.808 represents one hundred times the amount of menthol corresponding to 1 mil. (or Cc.) of the half-normal alkali solution, and B is the weight of acetylized oil taken.

The figure 0.021 is obtained as follows: In the acetylization of the oil, 1 molecule, or 156.16 Gms., of menthol becomes 1 molecule, or 198.176 Gms., of menthyl acetate, that is it acquires an increase of 42.016 Gms. The saponification of the ester, as shown above, requires for each molecule, or 198.176 Gms., of menthyl acetate, 1 molecule, or 56.11 Gms. of potassium hydroxide, or 2000 mils. (or Cc.) of half-normal alcoholic potassium hydroxide solution. Hence each liter of the half-normal alkali solution used in the saponification represents an increase af 21.008 Gms. in the weight of a certain amount of menthol in becoming menthyl acetate, or each mil. (or Cc.) of the half-normal alkali solution represents 0.021 Gm. increase in weight. $B - (A \times 0.021)$ is the weight of acetylized oil that is saponified minus the weight corresponding to the removed acetyl radical; in other words it is the weight of completely deacetylized oil equivalent to B Gms. of acetylized oil.

Japanese oil of peppermint, although rich in menthol (sometimes containing 79 per cent.), is not used medicinally, on account of its peculiar bitter and disagreeable taste.

Oil of peppermint differs from other oils in the variety of its color reaction with acids, as mentioned in the Pharmacopœia.

Oil of Pimenta or **Oil of Allspice** closely resembles oil of clove in its constitution, but has a lower specific gravity. It contains eugenol, $C_6H_3C_3H_5.OCH_3OH$, and a sesquiterpene, $C_{15}H_{24}$; but little or nothing is known regarding other constituents that give to the oil its peculiar odor. The official requirement is for not less than 65 per cent. by volume of eugenol, which is to be determined exactly as directed for the assay of oil of cloves.

Oil of Dwarf Pine Needles.—This oil, also known as Pine Needle Oil, is distilled on a commercial scale in the Tyrolese Alps from the fresh leaves of the dwarf pine. It occurs as a colorless or faintly yellowish liquid of pleasant aromatic odor, no portion of which distils below 170° C. (338° F.). The oil contains pinene, phellandrene, sylvestrene, cadinene and bornyl acetate, and is lævorotatory, the angle of rotation being from −5° to −10° in a 100 mm. tube at 15.5° C. (60° F.).

Oil of Rosemary.—The constituents of this oil are pinene, cineol, borneol, camphor and bornyl acetate, $C_{10}H_{17}C_2H_3O_2$. Several commercial varieties of the oil are known, as English, French, Italian

and Spanish, the Eperlé brand being considered the finest in this country. Oil of rosemary is dextrogyrate; it is soluble in ½ its volume or more of 90 per cent. alcohol, also in 10 volumes of 80 per cent. alcohol.

The Pharmacopœia requires that oil of rosemary shall contain not less than 2.5 per cent. of esters calculated as bornyl acetate and not less than 10 per cent. of total borneol, both determinations are made as directed for the determination of menthyl acetate and total menthol in oil of peppermint, except that different factors must be used, because the molecular weights of borneol and bornyl acetate are not identical with those of menthol and menthyl acetate, being 154.14 and 196.16 respectively. Each mil. (or Cc.) of half-normal alcoholic potassium hydroxide solution corresponds therefore to 0.07707 Gm. of borneol or 0.09808 Gm. of bornyl acetate.

The explanation of the formula given in the Pharmacopœia for calculation of the percentage of total borneol is practically identical with that given under Oil of Peppermint, simply substituting the figure 7.707 for 7.808.

Oil of Santal.—The official or East Indian oil of sandalwood is said to consist chiefly of alcohols, to which the name santalol and the formula $C_{15}H_{25}OH$ have been applied. The oil is said also to contain an aldehyde, called santalal, $C_{15}H_{24}O$, and a sesquiterpene. It is lævogyrate, its angle of rotation varying from $-15°$ to $-20°$ in a 100 mm. tube at 25° C. (77° F.), while inferior oils produced in Australia and the West Indies are all dextrorotatory.

Oil of santal may be adulterated with cedarwood oil, gurjun balsam oil, oil of copaiba and fatty oils, which can be detected by decreased solubility in 70 per cent. alcohol, the pure oil being soluble in 5 volumes of that liquid.

The pharmacopœia requires the presence of not less than 90 per cent. of alcohols, calculated as santalol, and the determination may be made according to the method given in the case of the oils of peppermint and rosemary. The molecular weight of santalol being 222.21, each mil. (or Cc.) of half-normal alcoholic potassium hydroxide solution used corresponds to 0.111105 Gm. of santalol, and to ascertain the percentage of santalol present, the number of mils. (or Cc.) of the alkali solution required must be multipled by 11.1105 (0.111105×100) and divided by the weight of acetylized oil taken less the number of mils. (or Cc.) of the KOH solution multiplied by 0.021.

The explanation of the formula given in the Pharmacopœia for calculating the percentage of total alcohols is practically identical with that given under Oil of Peppermint, simply substituting the figure 11.1105 for 7.808.

Oil of Sassafras.—The chief constituent of oil of sassafras is safrol, $C_{10}H_{10}O_2$, about 80 per cent., with a very small amount of

eugenol, about 10 per cent. of terpenes (pinene and phellandrene), and about 7 per cent. of camphor.

Safrol, at ordinary temperatures, is a colorless liquid of 1.108 specific gravity at 15° C. (59° F.); it is also found in Japanese camphor oil, from which it is now largely obtained. Sassafras oil is sometimes adulterated with camphor oil. Inasmuch as camphor oil contains all of the constituents found in sassafras oil, the detection of the former is exceedingly difficult, but its presence may be indicated by strong variations in the specific gravity and other physical properties. Under the name of artificial sassafras oil, fractions of camphor oil having a specific gravity similar to that of true sassafras oil are sold.

Official oil of sassafras is soluble in twice its volume of 90 per cent. alcohol and has an optical rotation of 3° to 4° in a 100 mm. tube at 25° C. (77° F.).

Oil of Spearmint.—In composition oil of spearmint differs radically from oil of peppermint, consisting principally of lævorotatory carvone and limonene, together with acetic acid and other volatile acids. Nelson, in 1912, isolated from American spearmint oil an alcohol, having the formula $C_{10}H_{17}OH$, partly in a free state and partly as an ester.

The Pharmacopœia requires that oil of spearmint shall contain not less than 43 per cent. of carvone, to be determined in the manner directed for the assay of oil of caraway.

Oil of Tar.—This oil, formed during the dry distillation of wood, is obtained from pine tar by fractional distillation. It is a complex mixture of hydrocarbons, phenols, acetic and other acids, and undetermined empyreumatic products present in tar.

Oil of Thyme.—The most important constituent of this oil is thymol, $C_{10}H_{14}O$, or $C_6H_3CH_3C_3H_7OH$, a monatomic phenol; the hydrocarbon cymene, $C_{10}H_{14}$, is also present, as well as very small quantities of pinene. The phenol content of the oil varies, as a rule, between 20 and 25 per cent., occasionally, but rarely, rising to 40 per cent. French, likewise German, oil of thyme contains chiefly thymol, although sometimes its isomer carvacrol is also present. The Spanish oil contains carvacrol and the phenol content rises as high as 50–70 per cent. at times. Oil of thyme is sometimes adulterated with oil of turpentine.

The Pharmacopœia requires the presence of not less than 20 per cent. of phenols, which may be determined as directed under Oil of Clove; more accurate results will, however, be obtained by the iodine method given on page 771.

In order to determine whether the oil contains thymol or carvacrol, the alkaline solution of phenol is separated from the oil, transferred to a separating funnel, and acidulated with sulphuric acid. After

the phenol has completely separated, the aqueous solution is drawn off and the oil set aside in a capsule in a cool place. If the oil consists of thymol, it solidifies upon standing, or crystallization may be induced by adding a fragment of a thymol crystal. If it consists of carvacrol the oil remains liquid. If both phenols are present it crystallizes partially.

Oil of Turpentine.—The official oil, commonly known as Spirit of Turpentine, is derived from American turpentine and consists almost wholly of dextrorotatory pinene, which, in the crude oil, is associated with rosin and other oxidation products, depending upon age and exposure.

The Pharmacopœia requires that 90 per cent. of the oil shall distil between 154° and 170° C. (309.2° and 338° F.), and gives a special test for the possible adulteration of oil of turpentine with mineral oil.

Oil of Turpentine, Rectified.—Since commercial oil of turpentine is unfit for internal administration, the Pharmacopœia directs that it be rectified by shaking it thoroughly with an equal volume of sodium hydroxide solution and then recovering about three-fourths of the oil by distillation, whereby rosin and other impurities are removed; the clear oil having been separated from the water, is dried by means of anhydrous calcium chloride and filtered.

Rectified oil of turpentine has a slightly lower specific gravity than the crude oil, and upon evaporation should not leave more than one-tenth as much residue as the latter; in other respects it is like the non-rectified oil.

Allied and Derivative Products.—The Pharmacopœia recognizes several compounds which, being allied to or directly obtained from volatile oils, should be considered at this point.

Benzaldehyde, C_7H_5O or C_6H_5COH.—This, the chief constituent of the volatile oil of bitter almond, and known also as artificial or synthetic oil of bitter almond, is now separately recognized. It differs from the natural oil of bitter almond mainly in the absence of all hydrocyanic acid.

It may be obtained from the volatile oil of bitter almond, peach, apricot, and other seeds by shaking the oil with 2 or 3 times its weight of a concentrated solution of acid sodium sulphite, whereby crystalline sodium benzalhydroxysulphonate is formed. The latter compound is washed with cold alcohol and treated with a strong solution of sodium carbonate, which causes the regeneration of benzaldehyde, and this is then rectified by distillation with steam. Synthetically, benzaldehyde is prepared either from benzyl chloride, $C_6H_5CH_2Cl$, or benzylene dichloride, $C_6H_5CHCl_2$, both of which may be obtained by treatment of boiling toluene with chlorine gas. In the case of

benzyl chloride, this compound is heated with either lead or barium nitrate, while a stream of carbon dioxide is passed through the mixture; the resulting benzyl nitrate decomposes with the formation of benzaldehyde and oxides of nitrogen. In the case of benzylene dichloride, this may be heated with water to 150° or 160° C. (302° or 320° F.), when benzaldehyde and hydrochloric acid are formed. In both cases the benzaldehyde produced is further purified by treatment with acid sodium sulphite, as stated above.

Like oil of bitter almond benzaldehyde is soluble in 300 parts of water, and when exposed to air readily oxidizes to benzoic acid. It is, however, not poisonous like the natural oil.

The Pharmacopœia gives appropriate tests for the presence of chlorinated products due to imperfect purification, and for the possible presence of nitrobenzene as an adulteration, and requires that official benzaldehyde shall contain not less than 85 per cent. of true C_6H_5COH, which is directed to be determined exactly in the same manner as for the assay of benzaldehyde in oil of bitter almonds, see page 774.

Camphor.—This term is applied to compounds having the composition $C_{10}H_{16}O$, which occur in a number of essential oils and are solid at ordinary temperature. They are no doubt the result of oxidation of hydrocarbons in the plant, and stand in the relation of a ketone to the alcohol borneol, $C_{10}H_{17}OH$. Official camphor is derived solely from the wood of the camphor tree of China and Japan. When camphor wood is heated in stills the camphor volatilizes and sublimes in the form of small grains, which come to this country as crude camphor. It is accompanied, as a by-product, by *oil of camphor;* a liquid of complex composition, containing not less than four hydrocarbons, pinene, phellandrene, dipentene, and cadinene, besides five oxidized bodies, cineol, camphor, terpineol, safrol, and eugenol.

In 1902 a patent was obtained in this country for the synthetic manufacture of camphor, the method being based on the interaction of anhydrous oil of turpentine with anhydrous oxalic acid at a temperature of 120°–130° C. (248°–266° F.). The chief products obtained are camphor and borneol, which may be separated by treatment with lime and subsequent distillation; the borneol can be converted into camphor by oxidation. Other methods for obtaining synthetic camphor are by action of acetates on pinene hydrochloride, production of camphene from pinene hydrochloride and conversion of this into isoborneol and finally into camphor, etc. Synthetic camphor thus made resembles the natural product closely in appearance and properties, having about the same specific gravity, melting point, and boiling point, but being optically inactive, while natural camphor is dextrorotatory to the extent of 41° and 42° in alcoholic solution in a 200 mm. tube at 25° C. (77°), the solution representing 10 Gms. in 100 mils. (or Cc.). The manufacture of synthetic camphor is now carried on to a limited extent.

Eugenol, $C_{10}H_{12}O_2$ or $C_6H_3(OH)(OCH_3).C_3H_5$.—Chemically this compound is also known as allylmethylpyrocatechol; it belongs to the class of phenols and is the chief constituent of oil of clove, besides being present in other oils. It is obtained by shaking oil of clove with an excess of 10 per cent. sodium hydroxide solution, whereby it is dissolved in the form of sodium eugenol. After washing the aqueous liquid with ether, it is decomposed with dilute sulphuric acid, the separated eugenol washed with sodium carbonate solution to remove adhering acid, and finally distilled.

Upon oxidation with potassium permangante eugenol yields vanillin. As it is used for the manufacture of the latter substance, it is sometimes abstracted from oil of clove, which thus loses materially in value.

Eucalyptol, $C_{10}H_{18}O$.—This compound, also known as cineol, constitutes the most important portion of the oils of cajuput and eucalyptus; it is present also in oil of rosemary and the volatile oil of santonica, *artimisia pauciflora*, is composed almost wholly of eucalyptol. Chemically it is a neutral oxide, but forms crystalline compounds with arsenic, hydrochloric and phosphoric acids. It may be obtained from the oils containing it by subjecting these to low temperatures and then draining off the adhering liquid, but this process is not very satisfactory; more desirable methods are to convert the eucalyptol into its crystalline compounds, as arsenate, hydrochloride or phosphate, by treating the oil with arsenic acid, hydrochloric acid gas or phosphoric acid, and then decomposing the product with warm water, when the liberated eucalyptol will rise to the surface and may then be washed with dilute alkali solution and distilled. Eucalyptol is optically inactive, which serves to distinguish it from oil of eucalyptus and many other volatile oils.

Menthol, $C_{10}H_{19}OH$.—This body, forming the chief constituent of oil of peppermint, is obtained now almost altogether from the Japanese oil by simple refrigeration, and is then purified by recrystallization. Its chemical character is that of a secondary alcohol, yielding by moderate oxidation with potassium dichromate and sulphuric acid a ketone, *menthone*, $C_{10}H_{18}O$, and combining with organic acids to form esters, such as menthyl acetate, benzoate, butyrate, formate, etc. By means of dehydrating agents, menthol is converted into the hydrocarbons menthene and dimenthene.

Menthol is only slightly soluble in water, but imparts to it its odor and taste; it is readily soluble in alcohol, ether, and chloroform. When triturated with an equal weight of camphor, hydrated chloral, or thymol, it liquefies. The presence of thymol in menthol may be detected by the appearance of a green color upon adding 3 drops of sulphuric acid and 1 drop of nitric acid to a solution of a few grains of menthol in 1 mil. (or Cc.) of glacial acetic acid.

Methyl Salicylate, $CH_3C_7H_5O_3$ or $C_6H_4(OH)COOCH_3$.—The name methyl salicylate is officially used to designate not only the ester, prepared synthetically, but also the oils distilled respectively from the bark of the sweet birch and the leaves of gaultheria or wintergreen, the Pharmacopœia demanding that the label shall indicate whether the product has been made synthetically or obtained by distillation from the two plants above mentioned.

Methyl salicylate is prepared synthetically by heating methyl alcohol and salicylic acid together in the presence of sulphuric acid. The reaction occurring may be shown by the equation $C_6H_4OHCOOH + CH_3OH + H_2SO_4 = C_6H_4OHCOOCH_3 + H_2O + H_2SO_4$; the sulphuric acid serving merely to remove the water as fast as eliminated. The newly formed methyl salicylate floats on the surface of the acid liquid and is subsequently rectified by distillation.

Neither the bark of betula alba (sweet birch) nor the leaves of gaultheria procumbens (wintergreen) contain much methyl salicylate, but both contain a glucoside, $C_{14}H_{18}O_8$, called gaultherin, which in the presence of water reacts with a ferment also present in both plants, to form the ester. The usual plan is to macerate the crushed bark of the sweet birch or the wintergreen leaves with water for twelve hours and then to distil the mixture; the reaction may be shown by the equation $C_{14}H_{18}O_8 + H_2O = C_6H_4OHCOOCH_3 + C_6H_{12}O_6$, dextrose being formed at the same time.

The distillates obtained from sweet birch bark and gaultheria leaves both contain besides methyl salicylate other bodies, such as an aldehyde, a paraffin, an alcohol and an ester having the formula $C_{14}H_{24}O_2$, all in small quantities. They have lower specific gravities than the synthetic product; the latter and oil of sweet birch are both optically inactive, while oil of gaultheria is slightly lævorotatory, not exceeding, however, $-1.5°$ in a 100 mm. tube at 25° C. (77° F.).

The Pharmacopœia gives the following synonyms for methyl salicylate: Oil of wintergreen, oil of sweet birch, oil of teaberry, and requires that the synthetic as well as the natural products shall contain not less than 98 per cent. of pure methyl salicylate, which is determined by saponifying the ester by means of half-normal alcoholic potassium hydroxide solution. An accurately weighed quantity of the sample is heated for two hours with an excess of the half-normal alkali solution and the excess of alkali then titrated with half-normal hydrochloric acid, each mil. (or Cc.) of the half-normal alkali solution consumed in the saponification corresponding to 0.07603 Gm. of the ester.

Monobromated Camphor, $C_{10}H_{15}BrO$ or $C_9H_{15}BrCO$.—This compound is obtained by heating camphor and bromine together in a flask or retort (preferably with the addition of water or chloroform) until reaction ceases, then allowing the yellowish solution to crystallize, heating until the mass becomes white, and recrystallizing from

alcohol or petroleum benzin. The reaction involves the formation of camphor dibromide, $C_{10}H_{16}OBr_2$, which splits up into camphor monobromide and hydrobromic acid, $C_{10}H_{16}OBr = C_{10}H_{15}BrO + HBr$, the latter distilling over with the water or chloroform.

Terebene.—This preparation is obtained by the action of concentrated sulphuric acid on oil of turpentine, the acid being gradually added to the oil; the mixture is allowed to stand for a day, after which the supernatant layer is removed, neutralized with chalk, and distilled. Terebene differs materially from oil of turpentine, consisting chiefly of dipentene and terpinene, with, perhaps, some cymol and camphene, but its composition will vary to some extent with the particular kind of oil of turpentine used in its manufacture, the products from American, French, and Russian oils not being identical. It is optically inactive, and in this respect differs from oil of turpentine, but it must not be overlooked that a fraudulent article may have been produced by careful mixture of dextrorotatory and lævorotatory oils of turpentine, resulting in an optically inactive liquid. The specific gravity of terebene varies from 0.860 to 0.865 at 25° C. (77° F.), and the Pharmacopœia gives the boiling point as between 160° and 172° C. (320° and 341.6° F.), whereas Power and Kleber (1894) claim that true terebene carefully prepared boils between 170° and 185° C. (338° and 365° F.). Like oil of turpentine, terebene is soluble in 3 volumes of alcohol. It should be preserved in a cool, dark place in well stoppered bottles.

Terpin Hydrate, $C_{10}H_{18}(OH)_2 + H_2O$.—This compound may be obtained by allowing a mixture of four parts of rectified oil of turpentine, 3 parts of 80 per cent. alcohol, and 1 part of nitric acid to stand in large, shallow dishes for several days; the crystals which have separated may then be drained, dried between filter paper, and recrystallized from 95 per cent. alcohol rendered slightly alkaline to remove adhering acid. The yield is about 12 per cent. of the weight of the oil of turpentine used, and the operation should always be performed in the cold, as, during hot weather, resinification of the oil will occur in place of the formation of crystals. Terpin hydrate, when fused or rendered anhydrous over sulphuric acid, yields terpin, $C_{10}H_{18}(OH)_2$, a dihydroxy alcohol, which, when distilled with moderately dilute sulphuric acid, loses water and is changed chiefly into terpineol, $C_{10}H_{17}OH$, a substance largely employed in perfumery on account of its very fragrant odor, resembling that of fresh lilacs.

Thymol, $C_{10}H_{14}O$ or $C_6H_3.CH_3.C_3H_7OH$.—This body, chemically known as methyl-propyl phenol, occurs in several volatile oils, and is obtained by treating the residue left upon distilling the oils below 200° C. (392° F.) with solution of sodium hydroxide, whereby thymol is dissolved as sodium thymol, $C_{10}H_{13}ONa$. When the solution has

become clear by subsidence, thymol is liberated by means of hydrochloric acid and purified by distillation and crystallization; if necessary it is also decolorized by treatment with animal charcoal.

The amount of thymol present in different oils varies considerably, and for commercial purposes it is, perhaps, all collected from ajowan oil, the volatile oil of the fruit of *ptychotis coptica*, which is said to contain from 45 to 55 per cent. of thymol; the oil of *monarda punctata*, commonly known as oil of horsemint, is said also to contain over 50 per cent. of thymol.

Thymol is sparingly soluble in water, requiring about 1100 parts for solution at 25° C. (77° F.), but is readily soluble in alcohol, ether, chloroform, and fixed and volatile oils. When triturated with an equal quantity of camphor, menthol or hydrated chloral, it liquefies.

Thymol Iodide, $C_{20}H_{24}O_2I_2$ or $(C_6H_2.CH_3.C_3H_7OI)_2$.—Chemically this compound is better known as dithymol diiodide, while commercially the names aristol and annidalin have been applied to it. It is obtained by adding an aqueous solution of iodine and potassium iodide to an alkaline aqueous solution of thymol, when condensation of 2 molecules of thymol occurs and 2 atoms of iodine are taken up in the phenolic groups simultaneously. The resulting bulky precipitate is washed with water and dried at a moderate temperature.

Although the Pharmacopœia has adopted the name thymol iodide for the compound, the name aristol, by which it was first introduced into medicine, will no doubt prevail. It is insoluble in water and glycerin and only slightly soluble in alcohol, but dissolves readily in ether, chloroform, and fixed and volatile oils. Thymol iodide contains about 45 per cent. of iodine, and is used both dry and in the form of ointments; in the latter case it is preferably rubbed up with a little expressed oil of almond before adding the solid fatty vehicle.

The Pharmacopœia requires the absence of alkalies and free iodine and of more than 5 per cent. of moisture, and demands that thymol iodide, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 43 per cent. of iodine, which is determined by fusing with sodium carbonate, oxidizing the resulting product with potassium permanganate, adding potassium iodide and dilute sulphuric acid, and finally titrating the liberated iodine with sodium thiosulphate solution.

The official assay involves first the formation of sodium iodide by reaction of thymol iodide with sodium carbonate when heated in the crucible; this is then converted into sodium iodate by action of the potassium permanganate in an alkaline medium. The next reaction is between the sodium iodate, potassium iodide and sulphuric acid, as shown by the equation $2NaIO_3 + 10KI + 6H_2SO_4 = 6I_2 + Na_2SO_4 + 5K_2SO_4 + 6H_2O$, iodic and hydriodic acids being liberated and then reacting set free iodine. Each molecule of thymol iodide will yield 2

molecules of sodium iodate, and these, as shown in the equation, will yield one-sixth of the iodine finally liberated; hence 1 mil. (or Cc.) of tenth-normal sodium thiosulphate solution used, corresponding to 0.012692 Gm. of the iodine, will correspond to 0.002115 (0.012692 ÷ 6 = 0.002115) Gm. of iodine derived from the thymol iodide. The number of mils. (or Cc.) of tenth-normal sodium thiosulphate solution required, when multiplied by 0.2115 (0.002115 × 100) and divided by the weight of thymol iodide taken, will express the percentage of iodine in the sample.

Vanillin, $C_8H_8O_3$ or $C_6H_3.OH.OCH_3.COH$.—This compound, chemically also known as methylprotocatechuic aldehyde, occurs naturally in vanilla bean, of which it is the odorous and active principle, to the extent of about 2 per cent. For commercial purposes it is made synthetically either from coniferin, a glucoside found in the cambium sap of pine trees, or from eugenol, the chief constituent of oil of clove. The latter source is preferred for economical reasons.

If made from eugenol, the latter is first converted into acetylisoeugenol, $C_{10}H_{11}(C_2H_3O)O_3$, by boiling with acetic anhydride, which is then oxidized with potassium dichromate or permanganate, yielding acetyl-vanillin. Upon treatment of the latter with potassium hydroxide solution, and concentration of the liquid, it is converted into vanillin. The mixture is filtered and the filtrate, after acidulation with sulphuric acid, shaken with ether, whereby the vanillin is removed and then purified by treating the ethereal solution with an aqueous solution of acid sodium sulphite for the removal of impurities, such as vanillic acid and vanilloylcarbonic acid. The purified ethereal solution upon evaporation at a low temperature yields vanillin.

If coniferin is to be used for the manufacture of vanillin, a concentrated solution of the same is slowly added to a moderately warm solution of potassium dichromate in water and sulphuric acid, the mixture being finally heated to boiling for three hours. The process involves the hydrolysis of the glucoside, yielding coniferyl alcohol and dextrose, the former being oxidized to vanillin with elimination of aldehyde, thus: $C_{16}H_{22}O_8 + H_2O = C_{10}H_{12}O_3 + C_6H_{12}O_6$; $C_{10}H_{12}O_3 + O = C_8H_8O_3 + C_2H_4O$. The vanillin may be recovered direct by passing steam through the mixture, or it may be extracted with successive portions of ether, after filtration of the liquid, and the ether recovered, leaving the vanillin in the form of a yellowish oily liquid, which congeals to a crystalline mass after a few days, and may be purified by solution in warm water and treatment with animal charcoal, and final recrystallization.

Vanillin is soluble in 100 parts of water at 25° C. (77° F.) and readily soluble in alcohol, ether, chloroform, and glycerin. It partakes of both aldehydic and phenolic characters and unites with bases to form saline compounds, which are decomposed upon addition of an acid with precipitation of the vanillin.

Vanillin has at times been extensively adulterated, and accounts have been published of gross sophistication. Benzoic acid, especially prepared for that purpose, acetanilid, boric acid, terpin hydrate, and cumarin, the odorous principle of tonka bean, have been employed, and adulteration to the extent of 50 per cent. has been found. Acetyl-isoeugenol has also been met with in commercial vanillin. The latter may be detected by the abnormal crystals revealed under the microscope and the beautiful red color developed with sulphuric acid, instead of the characteristic lemon-yellow color found in the case of pure vanillin.

RESINS.

Comparatively little was known until recently regarding the chemical composition of resins which occur in plants either alone or in combination with volatile oils as oleoresins or with gums as gum resins. Investigations have been in progress for some years in the hands of Prof. Tschirch, of Berne, Switzerland, and his colaborers, and much light has already been shed upon this rather obscure subject. This much has already been established, that resins are largely composed of organic acid esters or compound ethers of certain alcohols, to which latter the general name *resinol* has been applied; some of these alcohols give reactions similar to those characteristic of the tannins, and have therefore been designated as *resinotannols*. Thus we have benzo-resinol, storesinol, peruresinotannol, toluresinotannol, etc. Some resins have decidedly acid properties, while others are known to be anhydrides, as in the case of common pine resin or colophony, which is chiefly composed of abietic anhydride, $C_{44}H_{62}O_4$; one of the resins found in copaiba is a crystalline acid, called copaivic acid, having the elementary composition, $C_{20}H_{30}O_2$; the resin obtained from guaiacum wood and officially recognized as *guaiac*, consists largely (70 per cent. and over) of guaiaconic acid, $C_{19}H_{20}O_5$, to which the well known color reactions of guaiac with oxidizing agents are due.

Resin of Scammony consists almost wholly of scammonin, $C_{34}H_{56}O_{16}$, the anhydride of scammonic acid, which behaves like a glucoside. *Jalap resin* consists of two distinct resins which can be separated from each other by ether, the one insoluble in that menstruum, and constituting about 90 per cent. of the official resin, consists almost entirely of convolvulin, $C_{31}H_{50}O_{16}$, an anhydride possessing glucosidal properties and being colorless when pure. The official *resin of podophyllum* is a complex mixture, containing an acid called podophyllinic acid, insoluble in ether, and a substance to which the name podophyllotoxin has been given; the latter, which constitutes about 50 per cent. of the official product, is said to be the active purgative principle. Both these substances are soluble in chloroform, and may be separated by addition of ether to the chloroformic solution, which precipitates podophyllinic acid; upon evaporation of the ethereal solution podophyllotoxin is obtained.

CHAPTER LIX.

ORGANIC ACIDS.

Of the large number of compounds termed organic acids, only the few that are of special interest in pharmacy have been officially recognized. Organic acids are considered as derived from hydrocarbons or their alcohols, by replacement of hydrogen or hydroxyl by the univalent group carboxyl, COOH, and vary in their basicity as one, two, or three carboxyl groups may have been taken up, carrying with them one, two, or three atoms of replaceable hydrogen, as in the case of inorganic acids. The official organic acids are acetic acid, benzoic acid, citric acid, gallic acid, lactic acid, oleic acid, phenylcinchonic acid, salicylic acid, stearic acid, tannic acid, tartaric acid, and trichloracetic acid. Diluted hydrocyanic acid, although usually reckoned among the inorganic acids, is preferably considered at this point, since cyanogen is a carbon compound probably derived from hydrocarbons by substitution of nitrogen for hydrogen.

Acetic Acid, $HC_2H_3O_2$ or CH_3COOH.—This acid has already been considered in connection with the derivatives of cellulose on page 693.

Benzoic Acid, $HC_7H_5O_2$ or C_6H_5COOH.—Several methods are in use for obtaining this acid from benzoin, the balsamic resin from which it takes its name.

Both a dry and a wet process are employed for extracting the acid from the resin, in which it exists in a free state. The former is by sublimation, benzoin in coarse powder, which has been dried over lime, being heated in shallow iron pans covered with a porous diaphragm and connected with a suitable condenser, carefully regulated sandbath heat being used so as to avoid contamination of the acid with other products, partly the results of decomposition, which volatilize at a temperature approaching 200° C. (392° F.). The yield of acid by this method ranges from 6 to 8 per cent. of the weight of benzoin used, the fused resin retaining a considerable portion which can be recovered by the wet method; sublimed acid is never chemically pure, being always accompanied by a volatile oil to which the peculiar odor of the acid is due.

The wet method consists in treating powdered benzoin for some time with warm milk of lime, and finally boiling the mixture and filtering while hot. The filtrate is supersaturated with hydrochloric acid, the crude benzoic acid being allowed to crystallize and then purified by resolution in boiling water, with the addition of animal

charcoal, filtered and again crystallized. In this process calcium benzoate, $Ca(C_7H_5O_2)_2$, is first formed and then decomposed with hydrochloric acid, whereby benzoic acid is liberated while calcium chloride remains in solution, thus, $Ca(C_7H_5O_2)_2 + 2HCl = 2HC_7H_5O_2 + CaCl_2$. Benzoic acid obtained by this method is of fine white appearance, and devoid of the peculiar aroma of sublimed acid.

Of late years synthetic benzoic acid has been extensively produced, and the Pharmacopœia recognizes both the natural and synthetic products. The latter is made from toluene, $C_6H_5CH_3$, by passing chlorine gas into it while boiling until an increase in weight is no longer observed. Toluene is thereby converted into benzo-trichloride also known as trichlormethylbenzene, $C_6H_5CCl_3$, which liquid, when treated with water under pressure, is converted into benzoic and hydrochloric acids, thus, $C_6H_5CCl_3 + 2H_2O = C_6H_5COOH + 3HCl$; the benzoic acid is separated by straining, and washed with cold water until free from hydrochloric acid. It is important in this process that the chlorine gas be passed into the boiling toluene in diffused daylight, to avoid the formation of other products.

Benzoic acid can also be made from the urine of cattle and horses, which contains hippuric acid, or benzoyl glycocoll. By boiling hippuric acid with strong hydrochloric acid, the former absorbs water and is split up into benzoic acid and glycocoll or amidoacetic acid, thus: $CH_2(NH)(C_6H_5CO)COOH + H_2O = C_6H_5COOH + CH_2(NH_2)COOH$. Benzoic acid from this source is always accompanied by a fetid odor, which is removed by recrystallization and sublimation with benzoin.

The Pharmacopœia demands the absence of chlorine and cinnamic acid, giving appropriate tests for their presence and requires that benzoic acid, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 99.5 per cent. of pure hydrogen benzoate or absolute benzoic acid, which is determined by dissolving an accurately weighed quantity of the previously dried acid in diluted alcohol and titrating with tenth-normal barium hydroxide solution, each mil. (or Cc.) of which corresponds to 0.012205 Gm. of C_6H_5COOH. Barium hydroxide solution is ordered in place of potassium or sodium hydroxide solution because the absence of carbonate is essential, which condition is not readily attained in the latter solutions.

Citric Acid, $H_3C_6H_5O_7 + H_2O$ or $C_3H_4OH(COOH)_3 + H_2O$.—This acid belongs to the class known as fruit acids, and, although occurring in many plants, is obtained for use solely from lemons and limes. It is manufactured both in this country and Europe, on a large scale, from the juice of immature fruit, which contains from 6 to 8 per cent. of acid. The juice is first clarified by ebullition and then neutralized by addition of chalk, the resulting calcium citrate being washed with boiling water, in which it is sparingly soluble, and finally decomposed

by means of diluted sulphuric acid; the newly formed calcium sulphate is removed by straining, the solution of citric acid being concentrated and allowed to crystallize in large wooden vats lined with lead. If necessary, the crystals of citric acid are redissolved in water, the solution being subsequently filtered through animal charcoal, to remove color, and recrystallized.

As citric acid crystallizes better from solutions containing a little sulphuric acid traces of the latter are generally found in the commercial article. Small particles of metal found adhering to the crystals and deposited in solutions thereof are lead, derived from the crystallizing vats. The permissible limit of lead content is determined colorimetrically by comparing the color of an aqueous solution of an accurately weighed quantity of citric acid treated successively with sulphurous acid, sodium cyanide solution, stronger ammonia water and sodium sulphide solution and made up to 50 mils. (or Cc.), with the color of the same volume of an ammoniacal solution of lead nitrate of the strength of 0.00032 Gm. in 50 mils. (or Cc.) and treated exactly like the citric acid solution. The color of the citric acid solution should not be greater, when viewed downward in a glass cylinder against a white surface, than that of the lead solution. Contamination with crystals of tartaric acid can be readily detected by placing some of the crystals in a small dish with a little solution of potassium hydroxide; the crystals of citric acid slowly dissolve, while those of tartaric acid gradually become opaque, owing to the formation of acid potassium tartrate.

The Pharmacopœia demands 99.5 per cent. purity for citric acid, to be determined by titration with normal alkali solution. Citric acid being tribasic, each molecule, or 210.08 Gms., will require 3 molecules, or 168.33 Gms., of potassium hydroxide for neutralization, and hence each mil. (or Cc.) of normal KOH solution will correspond to 0.07002 Gm. of citric acid.

Solutions of citric acid gradually separate fungous growths; this can, however, be prevented by addition of 5 or 10 per cent. of alcohol.

Diluted Hydrocyanic Acid.—This acid, also known as prussic acid, is made on a large scale by decomposing a solution of potassium ferrocyanide with sulphuric acid, in a flask or retort, and conducting the resulting vapors into distilled water. In this process the following reactions occur: 1. The formation of hydroferrocyanic acid, thus, $K_4Fe(CN)_6 + 2H_2SO_4 = H_4Fe(CN)_6 + 2K_2SO_4$; 2. The decomposition of a further portion of potassium ferrocyanide by the newly formed acid in the presence of sulphuric acid, thus, $K_4Fe(CN)_6 + H_4Fe(CN)_6 + H_2SO_4 = 6HCN + K_2SO_4 + K_2Fe(Fe(CN)_6)$, hydrocyanic acid being evolved, while potassium sulphate and potassioferrous ferrocyanide, or Everitt's salt, remain in the flask or retort; the latter salt is white at first, but gradually changes to blue. Aqueous vapor, of course, passes over with the vapor of the acid, both of which are usually condensed in a Liebig

condenser interposed between the retort and the receiver. Distillation is continued until the volume of the mixture in the retort has been reduced to about one-half after which the distillate is assayed and sufficient distilled water added to bring the solution to the official standard of 2 per cent. strength.

Small quantities of hydrocyanic acid may be conveniently prepared by decomposing silver cyanide with diluted hydrochloric acid in proper proportions, as directed in the last Pharmacopœia. The equation $AgCN + HCl = HCN + AgCl$ shows that 1 molecule, or 133.89 Gms., of silver cyanide is capable of yielding 1 molecule, or 27.018 Gms., of hydrogen cyanide or absolute hydrocyanic acid, or 1 Gm. of silver cyanide will yield 0.2019 Gm. of the absolute acid.

Solutions of hydrocyanic acid are likely to deteriorate if kept on hand for some time, and since the acid is not used much now it is a rather unsatisfactory preparation. It should be kept in small, tightly closed amber-colored vials, and as a rule good sound corks will be found to fit more closely than glass stoppers. Various substances, such as diluted alcohol, sulphuric acid and hydrochloric acid, have been suggested for the preservation of the diluted acid, but thus far none has been found entirely satisfactory.

The Pharmacopœia requires that official diluted hydrocyanic acid shall contain not less than 1.9 per cent. nor more than 2.1 per cent. of hydrogen cyanide or absolute hydrocyanic acid, and not more than 0.1 per cent. of hydrochloric acid. The former is determined by titration with tenth-normal silver nitrate solution to the production of a slight permanent precipitate in the presence of potassium iodide test-solution as an indicator, each mil. (or Cc.) of the silver nitrate solution thus consumed corresponding to 0.005404 Gm. of pure HCN. The permanent turbidity occurs when all the hydrocyanic acid present is in combination as the double cyanide of potassium and silver, which is not affected by an excess of alkali, and the further addition of silver nitrate solution then causes decomposition, insoluble silver cyanide separating; the silver cyanide then reacts with the potassium iodide forming yellow silver iodide.

The amount of hydrochloric acid present is determined by adding an accurately weighed quantity of the diluted hydrocyanic acid to an excess of tenth-normal silver nitrate solution and determining the excess by titration with tenth-normal potassium sulphocyanate solution, each mil. (or Cc.) of the silver nitrate solution consumed corresponding to 0.003647 Gm. of hydrogen chloride or absolute hydrochloric acid. The number of mils. (or Cc.) of tenth-normal silver nitrate solution consumed in the official assay is ascertained by subtracting the number of mils. (or Cc.) of the potassium sulphocyanate solution required to produce a permanent color, from 25 mils. (or Cc.) of the silver nitrate solution, as only one-half of the filtrate is used in the final determination, and if from this remainder be subtracted the number of mils. (or Cc.) of tenth normal silver nitrate solution required

to produce a slight permanent precipitate in the determination of the hydrocyanic acid content, see above, the remainder will indicate the number of mils. (or Cc.) actually consumed by the free hydrochloric acid, which, if multiplied by 0.3647 (0.003647 × 100) and divided by one-half of the weight of diluted hydrocyanic acid originally taken (as only one-half was represented in the final determination), will express the per cent. of free hydrochloric acid present in the sample. In the determination of the hydrocyanic acid in the sample (see above) the hydrochloric acid present and neutralized by potassium hydroxide solution does not affect the silver nitrate solution up to the point of the appearance of a permanent turbidity.

A strong solution of hydrocyanic acid, known as Scheele's acid, contains 5 per cent. of absolute HCN, but is not used in this country for medicinal purposes.

The test with potassium hydroxide and ferrous sulphate, mentioned in the Pharmacopœia, is generall known as Scheele's test for hydrocyanic acid, and depends upon the formation of ferric ferrocyanide, or Prussian Blue, by alkali cyanides. The reactions occurring are as follows: 1. $HCN + KOH = KCN + H_2O$; 2. $6KCN + Fe(OH)_2 = K_4Fe(CN)_6 + 2KOH$; 3. $4Fe(OH)_3 + 12HCl + 3K_4Fe(CN)_6 = Fe_4(Fe(CN)_6)_3 + 12KCl + 6H_2O$. The first reaction results in the formation of potassium cyanide, and when ferrous sulphate is added to the solution containing an excess of potassium hydroxide, ferrous hydroxide is formed, a part of which is quickly oxidized by the air, and a part forms potassium ferrocyanide with the alkali cyanide present. Upon addition of the acid, the ferric chloride formed reacts with the potassium ferrocyanide, forming ferric ferrocyanide (Prussian Blue), which is precipitated.

Gallic Acid, $HC_7H_5O_5 + H_2O$ or $C_6H_2(OH)_3COOH + H_2O$.—This acid, also known as trihydroxybenzoic acid and dihydroxysalicylic acid, may be obtained either from nutgall or from tannin by treatment with diluted sulphuric acid at a boiling temperature; the mixture is then strained and the liquid set aside so that crystals may form, which are redissolved in hot water and decolorized with animal charcoal. After filtration, the filtrate is again set aside and allowed to crystallize. In either case the reaction occurring causes the absorption of the elements of water by the tannic acid.

Another method for manufacturing gallic acid, at one time largely used, is to form a thin paste of nutgall with water, which is exposed to the air in a warm place for a month, with occasional stirring and replacement of water that may evaporate; at the end of that time the paste is expressed, the liquid being rejected, and the residue boiled with distilled water for a few minutes; the mixture is filtered while hot through animal charcoal and allowed to crystallize. The crystals if not sufficiently free from color, are again dissolved in hot water, filtered as before, recrystallized, and dried.

Gallic acid is readily distinguished from tannic acid by its crystalline form and its lesser solubility in water, alcohol, and glycerin. Alkali citrates are said to increase the solubility of gallic acid in water to a marked degree. Its aqueous solution is, moreover, not precipitated by addition of albumen, starch, or gelatin solution, and the bluish-white precipitate formed upon addition of lime water is redissolved by an excess of gallic acid; a large excess of lime-water causes the liquid to assume a pink tint. Gallic acid causes no precipitation in alkaloidal solutions.

Medicinally, gallic acid is unlike tannic acid in so far that, externally applied, it exerts no astringent effect, although it readily controls passive hemorrhage when internally administered.

In connection with gallic acid its official derivative may also be considered:

Pyrogallol, $C_6H_6O_3$ or $C_6H_3(OH)_3$.—This compound, also known as pyrogallic acid and trihydroxybenzene, is a triatomic phenol and may be obtained by subliming previously dried gallic acid in an oil bath at a temperature of 200° or 210° C. (392° or 410° F.), the yield of this method amounts to about 30 per cent. If gallic acid be heated with two or three times its weight of water for half an hour at the above named temperature, under pressure in a suitable boiler, in such a manner that the liberated carbon dioxide can escape, a somewhat colored solution of pyrogallol will result, which, boiled with animal charcoal, filtered, and evaporated, yields an almost colorless crystalline mass, from which pure pyrogallol may be obtained; as the yield amounts to nearly 75 per cent. of the weight of gallic acid used, this process is preferred by manufacturers. In either case the chemical change is the same, gallic acid being split up into pyrogallol and carbon dioxide, thus: $C_6H_2(OH)_3COOH = C_6H_3(OH)_3 + CO_2$.

Pyrogallol is readily darkened, assuming a grayish tint, by exposure to air and light, owing to oxidation; hence it must be carefully preserved in tightly closed amber vials. It is very soluble in water, alcohol, and ether, and contamination with gallic acid may thus be detected.

As pyrogallol is poisonous, a derivative product has been introduced in its place, namely, *gallacetophenone*, or *gallactophenone*, prepared by heating a mixture of pyrogallol, zinc chloride, and glacial acetic acid to 148° C. (298.4° F.) and adding water to the fusion while hot; the resulting product may be recrystallized from boiling water. It occurs as a crystalline powder of dirty flesh-color, having the composition $C_6H_2(C_2H_3O)(OH)_3$.

Lactic Acid.—Official lactic acid, more specifically known as alpha-hydroxypropionic acid or ethyledene lactic acid to distinguish it from two other varieties of lactic acid known as ethylene lactic acid and sarcolactic acid, is a solution of optically inactive hydrogen lactate, $HC_3H_5O_3$, and lactic anhydrides, the total equivalent of which is

required by the Pharmacopœia to be not less than 85 per cent. nor more than 90 per cent. of absolute lactic acid, $C_3H_6O_3$ or CH_3CHOH-COOH. It is obtained by fermentation of a mixture of either milk sugar or inverted sugar (see page 724), milk, or cheese and water, at a temperature between 25° and 35° C. (77° and 95° F.); chalk or zinc oxide is added to neutralize the acid as fast as formed, since butyric acid is otherwise apt to be produced if much free lactic acid is present. The resulting calcium, or zinc lactate, is subsequently recrystallized and decomposed by means of sulphuric acid or hydrogen sulphide, the mixture filtered and the solution of lactic acid evaporated. Complete evaporation of the water is not practicable, since the lactic acid would undergo decomposition, the elements of water being split off and insoluble lactic anhydride formed; hence the Pharmacopœia recognizes a very strong solution in place of the absolute acid. The temperature is an important factor in the fermentation of milk, as below 25° C. (77° F.) acetic acid will be formed, above 35° C. (95° F.) butyric acid; hence the largest yield of lactic acid is produced between these two degrees of heat.

The Pharmacopœia directs that lactic acid shall be assayed by boiling an accurately weighed quantity of the acid for 20 minutes with an excess of normal potassium hydroxide solution and then titrating the excess of alkali in the boiling solution with normal sulphuric acid, each mil. (or Cc.) of the normal alkali solution consumed and containing 0.05611 Gm. of potassium hydroxide corresponding to 0.09005 Gm. of absolute lactic acid or anhydrides calculated as lactic acid.

The reaction between lactic acid, potassium permanganate, and sulphuric acid, mentioned in the Pharmacopœia, resulting in the development of an odor of aldehyde, is due to the oxidizing effect of the potassium permanganate, the lactic acid being split up into acetaldehyde, CH_3COH, and formic acid, HCOOH, which latter is then still further oxidized to carbon dioxide and water.

Oleic Acid, $HC_{18}H_{33}O_2$ or $CH_3(CH_2)_7CH.CH(CH_2)_7COOH$.—In the chapter on fats and fixed oils this acid has been mentioned as being found in nearly all liquid fats. It is usually obtained of variable quality in a crude state in the manufacture of candles, being then known as *red oil;* for pharmaceutical purposes the crude acid can be sufficiently purified by simply cooling the same to 5° C. (41° F.) and separating the liquid portion from palmitic and other acids. Such an acid is recognized in the Pharmacopœia. A still purer acid may be obtained by saponifying expressed oil of almond with lead oxide, dissolving the lead oleate in petroleum benzin and decomposing the solution with dilute hydrochloric acid; after removal of the benzin by evaporation, the oleic acid may be washed with water. When perfectly pure, oleic acid is colorless, odorless and tasteless, but rapidly becomes colored upon exposure to air and light.

Oleic acid may contain undecomposed fat, or mineral oil as an

adulteration, which are readily detected by boiling some of the acid with one-half its weight of monohydrated sodium carbonate and some water; the solution, while hot, should be clear or at most opalescent.

Phenylcinchonic Acid, $C_{16}H_{11}NO_2$ or $C_6H_5.C_9H_5N.COOH$.—This acid is perhaps best known by its copyrighted name "Atophan," and the official synonym, phenylquinoline-carboxylic acid, indicates its chemical character. Phenylcinchonic acid may be obtained by heating an alcoholic solution of aniline with a solution of pyroracemic acid, $CH_3.CO.COOH$, and benzaldehyde, C_6H_5COH, in absolute alcohol for 3 hours in a waterbath. It occurs in small colorless needles, or as a white or yellowish-white microcrystalline powder, insoluble in water and but slightly soluble in cold alcohol.

Salicylic Acid, also known as Orthohydroxybenzoic Acid, $HC_7H_5O_3$ or $C_6H_4(OH)COOH$.—Since the introduction of salicylic acid into medicine, nearly all thus used has been prepared synthetically from phenol (carbolic acid); small quantities are also obtained by treating oil of wintergreen with potassium hydroxide and decomposing the resulting potassium salicylate with an acid. Natural salicylic acid, obtained by the latter method, is preferred by some physicians; it commands a much higher price than the synthetic acid. In the synthetic process the first step is the manufacture of sodium carbolate, or sodium phenol, C_6H_5ONa, by saturating phenol with sodium hydroxide. This compound is then dried and treated with carbon dioxide, whereby sodium phenol carbonate is formed, thus, $C_6H_5ONa + CO_2 = NaC_6H_5CO_3$; this is heated in tightly closed vessels, or in retorts through which a stream of carbon dioxide is passing, to 130° C. (226° F.), when it is converted into sodium salicylate, $NaC_7H_5O_3$. This is the process now generally employed, and is a modification of Kolbe's original method, in which only one-half of the phenol was utilized, the remainder distilling over at a higher temperature. The crude sodium salicylate is dissolved in water and decomposed by means of hydrochloric acid; the resulting mixture is drained, washed with cold water, and finally dissolved in boiling water from which salicylic acid crystallizes on cooling and can be purified by solution in diluted alcohol, decolorized with animal charcoal, and recrystallized.

Salicylic acid is only slightly soluble in water, about 1 grain in a fluidounce, but its solubility is considerably increased by the addition of alkali acetates, citrates and phosphates, and also of borax, the solution made with the latter gradually turning bitter.

The Pharmacopœia states that if 0.5 Gm. of synthetic salicylic acid be dissolved in 10 mils. (or Cc.) of sulphuric acid at room temperature, not more than a light yellow color will develop, whereas if the natural acid, derived from oil of birch or oil of wintergreen, be treated in the same manner, a slightly brown color may be produced. It also requires

that salicylic acid, when dried to constant weight in a desiccator over sulphuric acid, shall contain not less than 99.3 per cent. of pure $C_7H_6O_3$, which is determined by dissolving an accurately weighed quantity of the previously dried acid in diluted alcohol and titrating with tenth-normal barium hydroxide solution, each mil. (or Cc.) of which corresponds to 0.013805 Gm. of pure salicylic acid. Barium hydroxide solution is ordered in place of potassium or sodium hydroxide solution because the absence of carbonate is essential, which condition is not readily attained in the latter solutions.

Salicylic acid furnishes several derivative products used in medicine, one of which is recognized in the Pharmacopœia under the name.

Phenyl Salicylate, $C_6H_5C_7H_5O_3$ or $C_6H_4(OH)COOC_6H_5$.—This compound is commercially better known as *Salol*, which was also formerly its official title. It can also be looked upon as a derivative of phenol, but as it is more closely allied to salicylic acid in its therapeutic effects, it is generally considered together with the same. Several methods are known for preparing phenyl salicylate, such as treating a mixture of sodium phenol and sodium salicylate with phosphorus oxychloride, or passing a slow current of phosgene (carbonyl chloride) into a warm mixture of the two salts; in both cases new sodium salts are formed as by-products, and the resulting phenyl ester is dissolved in alcohol and crystallized. A later and simpler process consists in heating salicylic acid, contained in a flask with long, narrow neck, in an oil-bath, to 220° or 230° C. (428° or 446° F.); air is excluded by passing a stream of carbon dioxide into the flask, the long neck of which permits only vapors of water and carbon dioxide to escape. The salicylic acid is first changed by heating into its anhydride, thus, $2HC_7H_5O_3 = (C_6H_4(OH)CO)_2O + H_2O$; this is then split up into phenyl salicylate and carbon dioxide, thus: $(C_6H_4(OH)CO)_2O = C_6H_5C_7H_5O_3 + CO_2$. The resulting compound is dissolved in alcohol and crystallized, as in the other methods.

Salol melts at a low temperature, about 42° C. (107.6° F.) and is very sparingly soluble in water, but readily so in alcohol. The Pharmacopœia gives a very simple test for the presence of uncombined phenol and salicylic acid; if 1 drop of ferric chloride test-solution be added to 10 mils. (or Cc.) of the filtrate obtained after shaking 1 Gm. of salol with 50 times its weight of distilled water, no violet color should appear.

Stearic Acid, $HC_{18}H_{35}O_2$ or $C_{17}H_{35}COOH$.—This acid, which is of very little use in pharmacy, except in the preparation of glycerin suppositories, is largely obtained in the manufacture of glycerin from tallow, by treatment with water and superheated steam, as explained on page 761. The commercial article is frequently impure, often consisting wholly of stearin; for pharmaceutical purposes it should,

at least, respond to the official requirement regarding the limit of undecomposed fat. Solubility in alcohol also serves to distinguish stearic acid from stearin.

Tannic Acid, $HC_{14}H_9O_9$ or $C_{13}H_9O_7.COOH$.—The official tannic acid is more specifically known as gallotannic acid, from its source, nutgall, to distinguish it from related compounds found in the bark of various oaks, chestnuts, etc.; it has, however, also been met with in the leaves of tea and sumac. The impossibility of obtaining tannic acid in the crystallized state has rendered the determination of its composition difficult. Owing to the fact that it is generally contaminated with variable proportions of glucose in weak combination, the view that tannic acid is a glucoside prevailed for a long time; it can be freed from glucose, however, as shown by Trimble, by treatment with lead acetate and hydrogen sulphide and subsequent extraction with acetic ether. In 1871 Schiff and in 1884 Etti announced as the result of their work that tannin from nutgalls must be looked upon as digallic anhydride, but more recent work by several investigators speaks against this view. It seems to be certain that tannic acid is not a simple uniform body, and E. Schmidt (1911) states that it seems to be a mixture of compounds of gallic acid of an anhydride character, mixed with varying proportions of glucogallic acid and other bodies. Still more recently the exhaustive investigations of Fischer and Freudenberg (1912 and 1913) lead them to consider tannic acid as an ether-like combination of glucose with five molecules of m-digallic acid. Evidently further work is necessary to establish the true character of this very interesting substance.

The subject of the various tannins was carefully studied in this country by the late H. R. Trimble, who laid down the results of his labors in a valuable and extended monograph, entitled *The Tannins*, from which work much of the information here given has been taken.

Different methods are employed by manufacturers for the extraction of gallotannic acid, giving rise to the varieties known as ether-, alcohol-, and water-tannin. Chinese or Japanese galls are preferred to the Turkish variety, on account of their richness in tannic acid, from 60 to 65 per cent., and greater freedom from coloring matters. The ether method yields the best product. The finely cut galls are first exhausted with water, at a temperature of 40° or 60° C. (104° or 140° F.); the infusion is allowed to cool, then filtered and intimately mixed with commercial ether by agitation. When the emulsion has separated, the upper ethereal layer, containing coloring matter, resin, fat, gallic and ellagic acids, is removed and the aqueous fluid, after concentration, under reduced pressure, in a still, to a syrupy consistence, is spread, when cool, on tin plates, which are placed on a steam table and covered with a wooden box; this causes the tannin to puff up and dry and gives rise to the peculiar spongy character of commer-

cial tannin. The so-called crystalline tannic acid of German manufacturers is obtained by introducing a very thick syrupy mass, prepared as above stated, into well tinned copper vessels, with a perforated bottom, through which the mass slowly drops in long threads on to heated revolving cylinders, where it dries, and is removed in the form of thin, needle-shaped particles.

Another plan is to extract the powdered nutgall with a mixture of ether four parts and alcohol one part, transferring the tannic acid to water by agitation with the latter, and then proceeding as before stated. This method is extensively employed.

Diluted alcohol is used in the preparation of alcohol-tannin by percolation, the tincture being concentrated and evaporated to dryness in a vacuum apparatus. Water-tannin is obtained by evaporating the aqueous infusion described above, to dryness, in a vacuum-pan. Neither of these products is as free from color or impurities as the first named or ether-tannin.

In 1893 Trimble suggested the use of acetone for the extraction of tannic acid from nutgall, and exhibited, at Chicago, a sample of the acid, almost white, prepared by this method. The advantages claimed for this solvent are cheapness, thorough penetration, and rapidity of action.

Glucose, the most persistent impurity found in tannin, can be removed completely, as suggested by Trimble, by treatment with lead acetate and hydrogen sulphide and subsequent extraction of the tannin with acetic ether.

Gallotannic acid differs markedly from oak-bark tannins in its behavior toward several reagents, thus, while with lime-water oak-tannins give a pink or red precipitate, gallotannic acid causes a blue precipitate; with bromine water gallotannic acid gives no precipitate, while oak-tannins cause a yellow precipitate; ferric chloride and ammonium hydroxide cause a green precipitate with oak-tannins and a blue one with gallotannic acid, etc. The blue color sometimes observed in the case of oak-tannins with ferric salts is due to the presence of a foreign substance, pure oak-tannins showing only a green color. (Trimble.)

Tannic acid is very soluble in water, but the solution soon deteriorates unless alcohol or glycerin be added; it is insoluble in ether and chloroform. It is incompatible with solutions of alkaloids, albumen, gelatin, glucosides and starch, causing precipitation. The Pharmacopœia requires that tannic acid, when dried to constant weight at 100° C. (212° F.), shall not lose more than 12 per cent. in weight, and also gives simple tests for the presence of dextrin, gum and resinous substances. All contact of tannic acid with metal, especially steel spatulas, must be avoided in the presence of moisture.

The term tannin is now applied to the whole group of vegetable astringents, while the name tannic acid has been reserved for the particular product derived from nutgalls. The classification adopted

by Trimble divides all tannins into two main groups, which may be distinguished from each other by the reactions above mentioned. All tannins should be soluble in water and precipitated by gelatin. The gallotannic acid group includes, besides nutgall tannin, the tannins found in chestnut wood, chestnut bark, pomegranate bark, and sumac, while the oak-tannin group comprises the tannins from different species of oak, from kino, gambir, krameria, tormentil, mangrove, and canaigre.

While, for technical purposes, the estimation of tannin in various tanning materials is often of importance, and is no doubt also valuable to chemical plant analysis, such determinations are not required in pharmacy. Advantage is taken of the well known property of tannin to form insoluble compounds with gelatin (as demonstrated in the preparation of leather), and this operation is included in all methods of assay thus far published. A complete account of Löwenthal's method for estimating tannin, as modified by Von Schroeder, will be found in the *National Standard Dispensatory*, 1916, p. 89.

Tartaric Acid, $H_2C_4H_4O_6$ or $(CHOH)_2(COOH)_2$.—This acid is even more widely distributed in the fruit of many plants than citric acid, occurring both in the free and combined state. For commercial purposes, it is obtained from crude or partially purified argols (see p. 568) by neutralizing the acid potassium tartrate in hot solution with chalk, whereby calcium and potassium tartrates are formed, and then decomposing the remaining potassium tartrate with calcium chloride; the resulting calcium tartrate is washed with water until tasteless and decomposed by digestion with sulphuric acid, when sparingly soluble calcium sulphate is formed and tartaric acid liberated, which latter enters into solution. After removal of the precipitated calcium sulphate by filtration, the solution of tartaric acid is concentrated and allowed to crystallize, the crystals, if necessary, being redissolved, digested with animal charcoal, and recrystallized.

Tartaric acid is rarely found in the shops in other than powder form, and, as a rule, is free from impurities. The official test for oxalic acid, by means of calcium sulphate solution, depends upon the insolubility of calcium oxalate in the presence of ammonium salts, whereas calcium tartrate is but slowly deposited under like conditions; an excess of ammonia must be avoided, hence the Pharmacopœia directs incomplete neutralization.

The Pharmacopœia requires almost absolute purity for tartaric acid, 99.5 per cent., which is determined by titration of an aqueous solution of the acid with normal potassium hydroxide solution, each mil. (or Cc.) of which corresponds to 0.07503 Gm. of pure hydrogen tartrate (absolute tartaric acid). As traces of lead may be present in tartaric acid, the permissible limit of this impurity may be determined colorimetrically exactly as in the case of citric acid.

Trichloracetic Acid, $HC_2Cl_3O_2$ or CCl_3COOH.—This acid has already been considered in connection with Acetic Acid on page 695.

The following organic acids, although not recognized in our Pharmacopœia, are of more or less interest to pharmacists; several of them are also official in foreign pharmacopœias.

Acetylsalicylic Acid. $C_9H_8O_4$ or $C_6H_4OCOCH_3COOH$.—This acid, better known as *Aspirin*, is obtained by heating salicylic acid with acetic anhydride or acetyl chloride to 150° C. (302° F.) in a flask under pressure, when either water or hydrochloric acid is split off, as acetic anhydride or acetyl chloride may have been used, as shown by the following equations: $2C_6H_4OHCOOH + (CH_3CO)_2O = 2C_6H_4OCOCH_3COOH + H_2O$ or $C_6H_4OHCOOH + CH_3COCl = C_6H_4OCOCH_3COOH + HCl$.

Aspirin occurs in colorless, odorless, needle-shaped crystals, having a slight acidulous taste and soluble in about 300 parts of water at 25° C. (77° F.). The name aspirin has been copyrighted in this country by the German patentees, who completely control its manufacture and sale. Tablets of aspirin have been found grossly adulterated with milk sugar, calcium phosphate, starch, etc., and pharmacists should avoid buying from irresponsible parties.

Camphoric Acid, $H_2C_{16}H_{14}O_4$ or $C_8H_{14}(COOH)_2$.—When camphor is oxidized by means of nitric acid, both camphoric and camphoronic acids are obtained. The following is the method usually pursued: About 150 Gms. of camphor are added to 2000 mils. (or Cc.) of 50 per cent. nitric acid contained in a long-neck flask provided with a reflux condenser, and the mixture heated on a boiling waterbath until colored vapors are no longer given off. When cool the liquid is filtered through asbestos, for the purpose of collecting the camphoric acid which has separated, and the filtrate made to yield an additional quantity of crystals by concentration to about one-fifth its volume, The crystals are dissolved in water with the aid of sodium carbonate, and the resulting sodium camphorate allowed to crystallize; after solution in water the salt is decomposed by means of hydrochloric acid, when the liberated camphoric acid will crystallize, and may then be further purified by solution in hot water, treatment with animal charcoal, and recrystallization. The acid mother-liquor, from which the crude camphoric acid is first separated, contains the second oxidation product, camphoronic acid, $C_6H_{11}(COOH)_3$.

Camphoric acid is soluble in 125 parts of water at 25° C. (77° F.), about $3\frac{1}{2}$ grains to the fluidounce, and in 10 parts of boiling water; also readily soluble in alcohol and ether.

Diethylbarbituric Acid, $C_6H_{12}O_3N_2$ or $(C_2H_5)_2C.CONH.CONH.CO$.—The commercial name *Veronal* is more familiar to pharmacists than

the chemical name of this acid. It may be obtained as a condensation product when diethylmalonic acid and urea are heated with sodium alcoholate for several hours at a temperature of 100° to 108° C. (212° to 226.4° F.); alcohol is liberated and sodium diethylbarbiturate formed, which latter is then decomposed with hydrochloric acid. The acid is official in the British Pharmacopœia under the name Barbitone.

Diethylbarbituric acid occurs in form of colorless, odorless, translucent leaflets or crystalline powder, having a slightly bitter taste, and is soluble in 170 parts of water. It is used as a hypnotic.

Meconic Acid, $H_2C_7H_2O_7 + 3H_2O$ or $C_5HO_2(OH)(COOH)_2 + 3H_2O$.—This acid is of interest chiefly as a constituent of opium, and also on account of its peculiar reaction with ferric chloride, which can be used as a test for preparations of opium; ferric meconate possesses a blood-red color, like that of ferric acetate and sulphocyanate, but may be distinguished from the former by its indifference to dilute hydrochloric acid, and from the latter by its indifference to mercuric chloride. Reducing agents, such as stannous chloride and alkali hypochlorites, discharge the color of ferric meconate. Meconic acid may be obtained by precipitating a concentrated infusion of opium with calcium chloride, decomposing the resulting calcium meconate with warm dilute hydrochloric acid and recrystallizing from water.

Oxalic Acid, $H_2C_2O_4 + 2H_2O$ or $(COOH)_2 + 2H_2O$.—Although this acid occurs in numerous plants, chiefly in the form of acid potassium oxalate, it is obtained for the market wholly by synthetic methods. If sawdust be made into a pasty mass with strong solution of potassium hydroxide, or potassium and sodium hydroxides, the mass then heated and kept at a temperature of 205° C. (401° F.) for one or two hours and dried, a gray powder of crude alkali oxalates will be obtained; by treatment with milk of lime, calcium oxalate results, which is then decomposed with sulphuric acid, and the solution of oxalic acid is concentrated and crystallized. A much larger yield is said to be obtained by heating sodium hydroxide with carbonic oxide to 100° C. (212° F.), whereby sodium formate, $NaHCO_2$, is produced, which is then further heated to 400° C. (752° F.), with exclusion of air as far as possible, and converted into sodium oxalate, from which the acid is liberated as above.

Oxalic acid is used in medicine only in the form of ferrous and cerous oxalates, but is a valuable reagent in chemical analysis.

Valeric Acid, also known as Valerianic Acid, $HC_6H_9O_2$ or $(CH_3)_2CH.CH_2.COOH$.—As this acid occurs in a free state in valerian root, it may be obtained by distilling the root with water, neutralizing the aqueous portion of the distillate with sodium hydroxide, and

decomposing this solution with sulphuric acid; it may then be purified by fractional distillation.

Commercially the acid is made by oxidation of amyl alcohol with a mixture of potassium dichromate and sulphuric acid, and neutralizing the distillate with sodium hydroxide; the resulting sodium valerate is decomposed by means of sulphuric acid, when the liberated valeric acid will rise as an oily layer. This is then freed from water by treatment with sulphuric acid, and carefully distilled. The reaction taking place may be illustrated thus: $3C_5H_{11}OH + 2K_2Cr_2O_7 + 8H_2SO_4 = 3HC_5H_9O_2 + 2K_2SO_4 + 2Cr_2(SO_4)_3 + 11H_2O$. Since a small portion of the amyl alcohol escapes oxidation, it is attacked by the newly formed acid and passes over into the distillate as a compound ether, known as *amyl valerate*, $C_5H_{11}C_5H_9O_2$; the name *apple oil* is given to this ester on account of its apple-like odor when diluted. When the acid distillate is neutralized with sodium hydroxide the amyl valerate separates as an oily liquid, and may be removed.

The solubility of valeric acid in not less than 26, and not requiring over 30 times its weight of water, affords a ready means of discovering certain impurities; it should also produce a clear solution with a slight excess of ammonia water.

The only use made of valeric acid in pharmacy is for the production of ammonium valerate in the manufacture of the elixir of the same name.

CHAPTER LX.

ALKALOIDS.

THE name alkaloids is applied to a large class of carbon compounds containing nitrogen, which are capable of neutralizing acids and forming salts. The basic properties of these compounds vary in intensity, some exhibiting but a feeble basic reaction, while others are capable of decomposing heavy metallic salts with the formation of metallic hydroxides. The term alkaloid was given to these so-called organic bases on account of their similarity in chemical character to alkalies, alkaloid meaning alkali-like.

Since the discovery of basic principles in both living and dead animal tissues the name alkaloids has generally been restricted to those nitrogenous bases derived from plants, the term *leucomaines* having been selected for the basic substances found in living animal tissues and *ptomaines* for those produced during putrefaction of dead animal tissues; the last named are still sometimes called cadaveric alkaloids. Chemists go even a step further by subdividing vegetable bases and reserving the name alkaloid for all those shown to be derived from pyridine, C_5H_5N, or quinoline, C_9H_7N, two simple bases found in coal tar.

The discovery of alkaloids occurred early in the last century, when Sertürner, a German apothecary, in 1817, demonstrated the basic character of a substance obtained by him, in 1806, from opium, now known to us as morphine. Since then the number of alkaloids determined has increased rapidly, although their occurrence is confined to comparatively few plant families, for instance, the apocynaceæ, leguminosæ, liliaceæ, loganiaceæ, papaveraceæ, ranunculaceæ, rubiaceæ, rutaceæ, solanaceæ, umbelliferæ, and perhaps one or two others. Sometimes the same alkaloid is found in more than one family, as in the case of the alkaloid berberine, but the occurrences are rare. As a rule, alkaloids are not restricted to special parts of plants; while present to a much larger extent in the root, bark, fruit, and seed of different plants, in a few cases the leaves are the chief source, and in some cases the same alkaloids are found in every part of the plant. In order to distinguish the basic from neutral vegetable principles a different terminology has been adopted for the two classes, which has been maintained in the Pharmacopœia, and serves an excellent purpose. The ending *ine* (Latin *ina*) is applied to all basic plant products, while the ending *in* (Latin *inum*) is given to all neutral principles.

While all alkaloids contain nitrogen, a few do not contain oxygen. The latter are, as a rule, colorless liquids when freshly obtained and not exposed to the air, and can be distilled without decomposition; they are generally characterized by a peculiar strong odor, as in the

case of coniine, nicotine, and sparteine. Alkaloids containing oxygen are generally without odor and, as a rule, crystallizable, a few also occurring in the liquid state. With the exception of codeine, colchicine, pelletierine, and physostigmine, alkaloids are difficultly soluble in water, but all dissolve readily in alcohol, and some, but not all, dissolve in amyl alcohol, benzene, chloroform, ether, and ethyl acetate. Vegetable bases do not all possess the same saturating power, for while the majority are monacid in their character, several well defined diacid bases are known. When brought together with acids they do not, like inorganic bases, cause the displacement of basylous hydrogen with the formation of water, but form salts by simple addition. Inasmuch as alkaloids are closely related to ammonia and often designated as substituted ammonias, it has been suggested that the same view be taken in regard to the formation of their salts with acids, as in the case of ammonia, namely, that when in solution in water they take up the elements of water and then unite with the acids with elimination of water, as, for instance, $NH_3 + H_2O = NH_4OH$ and $NH_4OH + HCl = NH_4Cl + H_2O$; $C_{17}H_{19}NO_3$ (morphine) $+ H_2O = C_{17}H_{20}O_3NOH$ and $C_{17}H_{20}O_3NOH + HCl = C_{17}H_{20}O_3NCl + H_2O$. This view is not expressed in the formulas and the nomenclature of the Pharmacopœia, but may in the course of time become more generally accepted. In regard to the naming of salts formed by the union of alkaloids with acids, it is customary in the case of oxygen acids to follow the usual rule, thus: acetates, citrates, nitrates, phosphates, sulphates, etc., but in the case of halogen acids, the proper name would seem to be obtained by changing the termination *ic* of the acid into *ide* for the salt, thus hydrobromide, hydrochloride, hydrocyanide, etc.

In nature alkaloids rarely occur in a free state, being usually associated with an acid, which, in some instances, is a peculiar acid characteristic of the plant in which it is found, as quinic acid of the cinchona barks, meconic acid in opium, etc.; many alkaloids occur in the plant as tannates. Occasionally the alkaloid exists partly in combination and partly in the free state, as in the case of hydrastine. For their extraction various methods are employed; either the finely comminuted drug is exhausted with acidulated water, whereby the alkaloid is brought into solution as a new salt, which can then be decomposed and precipitated by means of an alkali and further purified by resolution in some appropriate solvent, filtration through animal charcoal, and crystallization; or the drug may be exhausted with a neutral solvent, such as alcohol or diluted alcohol, the resulting tincture being acidulated, evaporated to remove fats, resins, etc., filtered, treated with water, and precipitated and purified as stated above. Advantage is taken of the difference in solubility between free alkaloids and their salts to separate and purify the product by the use of immiscible solvents, such as water and petroleum benzin, water and chloroform, water and ether, etc., whereby the alkaloid can be alternately transferred, in a combined or free state, from one fluid to another; this necessitates, of course, provision for bringing the liquids

into intimate contact by agitators. This method, which is extensively employed in the assay of alkaloidal drugs, is termed by analysts the "shaking out process," because, on a small scale, the transfer is made in glass separators by rotation or shaking. In large operations, such as the manufacture of the cinchona alkaloids and others, kerosene or gasolin, closely allied to benzin, is now extensively employed on account of its solvent capacity, its cheapness, and ready separation from watery fluids. In the case of alkaloids which are volatile, the drug is placed in a still with some water, and, by the addition of a fixed alkali, the alkaloid is liberated, and, with the aid of heat, passed over into a receiver containing acidulated water, when, having been obtained as an acid salt, it can be further purified and isolated by one of the methods before mentioned.

To determine the presence of an alkaloid in any drug, the simplest plan is to macerate a small portion of the finely powdered article with about ten times its weight of Prollius' fluid, a liquid of remarkable penetrating power, composed of ether 325 mils. (or Cc.), alcohol 25 mils. (or Cc.), and stronger water of ammonia 10 mils. (or Cc.). The maceration should be conducted in a well closed flask, for several hours, with frequent agitation, after which some of the clear liquid is decanted into a glass separator (see page 173) containing some 5 per cent. sulphuric acid, and, by means of careful but active rotation, any alkaloid present is transferred to the acid fluid; upon withdrawing this and warming on a waterbath to remove ether and alcohol, the addition of any of the general reagents mentioned below will produce a cloudiness or precipitate if alkaloids have been extracted.

Although particular alkaloids are only found in certain plants or species of plants, it often happens that several alkaloids are present in the same plant, ranging from 2 in nux vomica to 21 in opium and 32 in cinchona; rarely, however, does the number exceed 4. When pure, alkaloids are, as a rule, crystallizable, excepting the amines or liquid bases, without color, and have a definite melting-point, which latter is an important test of purity; their different solubilities have already been referred to. In solution, whether free or in a combined state, they are precipitated by a number of substances which are known as alkaloidal class reagents, and therefore incompatible with them in prescriptions. Such reagents are tannic acid, picric acid, and mercuric chloride; besides these, the following tests for the presence of alkaloids are known by special names—*Mayer's reagent*, a solution of potassium mercuric iodide (see United States Pharmacopœia, page 538), *Marme's* reagent, a solution of potassium cadmium iodide, *Dragendorff's reagent* a solution of potassium bismuth iodide, *Scheibler's reagent*, phosphotungstic acid, *Sonnenschein's reagent*, phosphomolybdic acid, *Wagner's reagent*, a solution of iodine together with potassium iodide, and others. The precipitates caused by these reagents in alkaloidal solutions are in some cases analogous to compounds formed in solutions of the inorganic bases, thus the alkaloidal periodides closely resemble potassium triiodide in composition, with the exception that some alkaloids have

the power to combine with three, four, or even eight atoms of iodine. Many alkaloids give characteristic color reactions with acids and other reagents, by means of which their identity may be established; some of these reactions will be mentioned further on, in connection with the individual alkaloids. Very complete information regarding the behavior of alkaloids toward reagents as well as their source, solubilities, etc., is to be found in Sohn's *Dictionary of the Active Principles of Plants* (1894).

Until about 20 or 25 years ago comparatively little was known regarding the chemical constitution of alkaloids and their relation to each other. Since then numerous investigations have been actively carried on along these lines, and much valuable information has been published.[1] Such investigations will eventually lead to the successful synthetic production of numerous natural alkaloids, as is already the case, on a commercial scale, with cocaine and codeine.

The following natural alkaloids are recognized in the Pharmacopœia in an uncombined state: *Aconitine, Atropine, Cocaine, Codeine, Colchicine, Hydrastine, Morphine, Quinine, Strychnine, Theophylline,* and *Veratrine. Caffeine,* although possessing but very feeble basic properties, must nevertheless also be placed in this class; by some authorities it is not considered an alkaloid at all, since it is not precipitated by potassium mercuric iodide solution and other class reagents.

Salts of the following natural alkaloids are officially recognized: Atropine, Caffeine, Cinchonidine, Cinchonine, Cocaine, Codeine, Emetine, Hydrastine, Hyoscyamine, Morphine, Pelletierine, Physostigmine, Pilocarpine, Quinine, Scopolamine, Sparteine, Strychnine and Theobromine; also salts of the following synthetic derivatives: Apomorphine, Betaeucaine, Cotarnine, Diacetylmorphine, Ethylmorphine and Hydrastinine.

THE OFFICIAL ALKALOIDS AND ALKALOIDAL SALTS.

Aconitine, $C_{34}H_{47}O_{11}N$.—This very poisonous alkaloid is found in the root of Aconitum Napellus, where it exists in combination with aconitic acid to an extent varying from 0.5 to 1.15 per cent. It is usually extracted by means of alcohol containing about ½ per cent. of tartaric acid. The alcoholic tincture is concentrated at a low temperature, mixed with water, and afterward with ether or petroleum benzin to remove fatty matter and resin, and finally precipitated by an excess of potassium or sodium carbonate. Amorphous bases are kept in solution by the alkaline liquid, and the washed precipitate is dissolved in ether and allowed to crystallize. By recrystallization from alcohol the alkaloid is eventually obtained pure.

[1] The excellent work of Guareschi, translated from the Italian by Kunz-Krause, 2 vols., 1896 and 1897, and the more recent works by Pictet, translated from the French by Wolffenstein, and by Brühl, Hjelt, and Aschan, 1900, offer a very comprehensive compilation of everything pertaining to plant alkaloids up to recent times. Unfortunately, these books have not yet been translated into English, and are accessible only to those familiar with the German language.

Commercial aconitine still occurs in both the amorphous and crystalline forms, but only the latter variety should be used, as the amorphous product contains derivatives considerably less active (10 or 15 times) than the crystallized alkaloid. The formula adopted by the Pharmacopœia for aconitine is that proposed by Freund and Beck in 1895, whereas the British Pharmacopœia assigns to the alkaloid the formula $C_{33}H_{43}NO_{11}$, suggested by Dunstan and Ince in 1891.

Aconitine melts, when rapidly heated, at 195° C. (383° F.), but if slowly heated it decomposes and melts at 182° C. (359.6° F.). It is very sparingly soluble in water and petroleum benzin, but dissolves readily in alcohol, ether, benzene, and chloroform. Sulphuric acid is without effect on aconitine, but if a crystal of ammonium vanadate be added, an orange color is produced. Aconitine may be distinguished from atropine and pseudaconitine by not yielding a violet color if a very small quantity be heated with a few drops of fuming nitric acid to dryness and the residue, when cool, then treated with alcoholic solution of potassium hydroxide. It is used chiefly for the preparation of a 2 per cent. oleate, but is occasionally also prescribed for internal use. It must be handled with great care, the average adult dose being about 0.00015 Gm. or about $\frac{1}{410}$ grain.

Apomorphine Hydrochloride. $C_{17}H_{17}O_2NHCl + \frac{1}{2}H_2O$.—Apomorphine may be classed among the so-called artificial alkaloids, being obtained by the action of hydrochloric acid on morphine or codeine. The process consists in heating either alkaloid with about 20 parts of pure hydrochloric acid in a sealed tube for several hours in an oil bath to between 140° and 150° C. (284° and 302° F.). After cooling the liquid contained in the tube is diluted with water, when, upon the addition of an excess of sodium bicarbonate, apomorphine will be precipitated; the mixture is filtered and the new alkaloid extracted from the residue by means of ether or chloroform. The reaction occurring in the case of morphine appears to be simply an abstraction of the elements of water; thus, $C_{17}H_{19}NO_3 - H_2O = C_{17}H_{17}NO_2$; in the case of codeine, however, an intermediate product, chlorocodid, is formed, which is further split up into methyl chloride and apomorphine, thus, $C_{18}H_{21}NO_3 + HCl = C_{18}H_{20}ClNO_2 + H_2O$; $C_{18}H_{20}ClNO_2 = C_{17}H_{17}NO_2 + CH_3Cl$. If a few drops of hydrochloric acid be added to the ethereal or chloroformic solution above mentioned, apomorphine hydrochloride will separate in a crystalline form, and may be recrystallized from boiling water. The salt must be thoroughly dried over sulphuric acid and carefully protected against moisture, air, and light, otherwise it soon assumes a green color, due to oxidation.

Apomorphine hydrochloride is always dispensed in the form of aqueous solutions, and amber vials should be used for the same; the gradual green coloration of the solution can be prevented by addition of a few drops of hydrochloric or acetic acid. A solution of this salt may be readily distinguished from one of morphine hydrochloride by being colored red by addition of dilute ferric chloride

solution, whereas the morphine solution will be colored blue. Apomorphine hydrochloride, when shaken with ether (0.1 Gm. to 10 mils. (or Cc.)), should not develop a pale reddish color, showing the absence of decomposition products, and should be rejected if it imparts at once an emerald-green color to 100 times its weight of distilled water when shaken with it.

Atropine. $C_{17}H_{23}O_3N$.—This alkaloid belongs to the class known as mydriatic alkaloids, so named on account of their property of causing dilatation of the pupil of the eye, which occur in belladonna, duboisia, hyoscyamus, scopola, and stramonium, and include atropine, belladonnine, hyoscyamine and scopolamine; daturine and duboisine, formerly considered as distinct alkaloids, are now known to be identical with atropine and hyoscyamine respectively. Atropine, and hyoscyamine have the same percentage composition, and the last named can be converted into the first by the action of alkalies in alcoholic solution. All three alkaloids are easily decomposed by strong acids and alkalies.

Atropine is found chiefly in belladonna, being obtained preferably from the root, as the latter is richer in alkaloid and free from chlorophyll. The finely powdered root is exhausted with alcohol, and the percolate mixed with calcium hydroxide to decompose the natural salt of atropine and liberate the alkaloid, which remains in solution; after filtration, the filtrate is acidulated with diluted sulphuric acid, concentrated to remove alcohol, fat, and resin, and treated with alkali carbonate in excess. The precipitated atropine is removed, washed with water, and dissolved in alcohol; to this alcoholic solution water is added, drop by drop, to incipient turbidity, and the alkaloid allowed to crystallize. Other bases present remain in the mother-liquor, but small quantities of hyoscyamine always accompany the commercial article.

Atropine is a monacid base possessing marked alkaline properties; it is capable of decomposing mercuric and mercurous chloride with the formation of the respective oxides; it also reddens phenol phthalein paper and restores the blue color of reddened litmus.

A characteristic reaction of atropine and its salts is the production of an intense violet color, if evaporated to dryness with a few drops of nitric acid in a porcelain dish and then adding alcoholic potassium hydroxide solution and a fragment of potassium hydroxide to the yellow residue.

Commercial atropine is usually contaminated with small quantities of hyoscyamine, from which it is freed with difficulty and which has the effect of lowering the melting point of the alkaloid. Pure atropine melts at 115.8° C. (240.4° F.), but the commercial product usually melts between 114° and 116° C. (237.2° and 240.8° F.), which is caused by the presence of hyoscyamine having a melting point of 108° C. (226.4° F.).

The alkaloid atropine is very rarely used, except for the preparation of atropine oleate, a 2 per cent. solution.

Atropine Sulphate. $(C_{17}H_{23}O_3N)_2H_2SO_4 + H_2O$.—This salt may be prepared either by adding atropine slowly to a mixture of sulphuric acid and alcohol or by dissolving atropine mixed with water by means of diluted sulphuric acid. In either case a perfectly neutral solution must be obtained, which is then evaporated to dryness, at a temperature below 40° C. (104° F.). Some of the commercial salts show an acid reaction when dissolved in water, and are, therefore, unfit for use.

Betaeucaine Hydrochloride, also known as Eucaine Chloride or Eucaine B. $C_{15}H_{21}O_2NHCl$ or $C_5H_7N(CH_3)_3O(C_6H_5CO)HCl$.—This salt of a synthetic derivative of piperidine, $C_5H_{11}N$, is obtained by first acting on acetone with ammonia when, as a result of condensation, diacetoneamine, $C_6H_{13}NO$, is formed with liberation of water, which is then treated with paraldehyde producing vinyldiacetoneamine, $C_8H_{15}NO$; by reduction with metallic sodium vinyldiacetonealkamine, $C_8H_{17}NO$, is obtained, which after treatment with benzoyl chloride, C_6H_5COCl, yields trimethylbenzoxypiperidine or beta-eucaine. By dissolving the base in diluted hydrochloric acid, the salt is formed and may be crystallized. The name benzamine has been adopted for the free base in the British Pharmacopœia, instead of beta-eucaine.

Beta-eucaine hydrochloride occurs as a white, crystalline, odorless powder, which is soluble in 30 parts of water. The Pharmacopœia requires that the salt, when dried to constant weight at 100° C. (212° F.) shall contain not less than 99 per cent. of trimethylbenzoxypiperidine hydrochloride, which is determined by titrating a solution of the previously dried salt in perfectly neutral alcohol with tenth-normal potassium hydroxide solution, each mil. (or Cc.) of the latter consumed corresponding to 0.028365 Gm. of $C_{15}H_{21}NO_2HCl$.

Caffeine, $C_8H_{10}O_2N_4 + H_2O$ or $C_5H(CH_3)_3O_2N_4 + H_2O$.—This feebly basic substance occurs in a number of plants belonging to different natural orders; thus, in coffee, tea, kola, and paullinia, associated with tannin, and varies in amount from less than 1 to 5 per cent. of the dried material. For commercial purposes it is usually obtained from powdered coffee beans, not roasted, or preferably the fine, unsalable particles of tea leaves (tea leaves being also much richer in caffeine) by exhausting the same with hot water, adding a solution of lead acetate in slight excess, whereby tannin and coloring matters are precipitated, filtering, adding ammonia water to remove excess of lead salt, and again filtering. The filtrate is concentrated, hydrogen sulphide added to remove any lead still remaining, filtered, and further evaporated to the crystallizing point. Milk of lime is also sometimes used to remove tannin, fat, coloring matter, etc., and is added to the powdered material, the mixture being then exhausted with warm 80 per cent. alcohol; the percolate is diluted with about one-sixth its volume of water and distilled to recover the alcohol. The aqueous residue is filtered and crystallized. If necessary, the product is redissolved, filtered through bone-black, and again crystallized.

Caffeine is very soluble in boiling water, 2 parts, and also in chloroform, 8 parts, but requires about 46 parts of water for solution at 25° C. (77° F.), which quantity is very materially reduced, however, by the presence of certain other substances, such as sodium benzoate, bromide, salicylate, and cinnamate, and even antipyrine.

The caffeine derived from different sources is identical, although the names theine and guaranine are still occasionally used.

Caffeine is a derivative of xanthine, as shown by the murexide reaction mentioned below, being known as trimethyl xanthine $C_5H(CH_3)_3O_2N_4$, and sometimes also called methyl-theobromine. It has been prepared synthetically by the action of methyl iodide on theobromine, $C_5H_2(CH_3)_2O_2N_4$, a basic substance found in cacao beans.

When treated with chlorine water or hydrochloric acid and potassium chlorate, as directed in the Pharmacopœia, caffeine yields, upon evaporation to dryness, a substance known as *amalic acid*, which, in the presence of air and ammonia, forms murexoin or tetramethyl murexide, $C_8(CH_3)_4N_5O_6(NH_4)$, of a rich purple color; this test is characteristic of caffeine and theobromine.

Caffeine Sodio-benzoate.—This preparation is not a double salt, as the name might lead one to suppose, but is merely an intimate mixture of caffeine and sodium benzoate, obtained by triturating a mixture of the two substances with sufficient alcohol to form a smooth paste, and then drying this by exposure in a moderately warm place; the dry mass is finally reduced to powder. It is soluble in a little more than its own weight of water, due to the presence of the sodium benzoate.

The Pharmacopœia requires that caffeine sodio-benzoate, when dried to constant weight at 80° C. (176° F.), shall contain not less than 46 per cent. nor more than 50 per cent. of anhydrous caffeine, and gives directions for determining the proportions of both the caffeine and sodium benzoate in the mixture.

Caffeina Citrata. Citrated Caffeine.—Under this name the Pharmacopœia recognizes an intimate mixture, by some declared to be a definite, but feeble, chemical compound, obtained by dissolving 50 Gms. of caffeine in a solution of 50 Gms. of citric acid and 100 mils. (or Cc.) of hot water, and evaporating the solution to dryness on a waterbath, with constant stirring. The resulting product is a white powder with acid taste and reaction. With 3 parts of water it forms a clear, syrupy liquid, from which caffeine is precipitated upon addition of 5 parts of water; when 25 parts of water have been added, however, the precipitate is redissolved. The presence of tartaric acid may be determined by the development of a brown or black color, if 0.25 Gm. of the citrated caffeine be heated with 5 mils. (or Cc.) of sulphuric acid for 15 minutes on a waterbath.

The Pharmacopœia requires that citrated caffeine, when dried to constant weight at 80° C. (176° F.), shall contain not less than 48 per

cent of anhydrous caffeine, which is determined by dissolving an accurately weighed quantity of the previously dried mixture in water, adding sodium hydroxide solution and shaking out the separated caffeine with three or more successive portions of chloroform; upon evaporation of the combined chloroform solutions, the residue is dried at 80° C. (176° F.).

The Pharmacopœia also directs the preparation of effervescent citrated caffeine to contain 4 per cent. of the salt; this preparation is made according to the general directions for granular effervescent salts, and has been considered on pages 473 and 476; it should contain not less than 1.9 per cent. of anhydrous caffeine.

Cinchonidine Sulphate. $(C_{19}H_{22}ON_2)_2H_2SO_4 + 3H_2O$.—Cinchonidine is one of the four important alkaloids found, among a large number (32), in cinchona bark, and occurs in greater proportion in the so-called red bark, derived from cinchona succirubra, than in others. The sulphate is obtained from the mother-liquors left in the manufacture of quinine sulphate, and is purified by fractional crystallization. The official salt, containing but three molecules, 7.29+ per cent., of water of crystallization, is the result of using a hot, concentrated solution, for if the salt be crystallized from weaker solution it will contain six molecules, or 14.6 per cent. of water.

Absolute purity of the commercial salt is not practicable, nor demanded by the Pharmacopœia, hence a faint blue fluorescence is observed in solutions of the salt made with diluted sulphuric acid. When dried to constant weight at 100° C. (212° F.), cinchonidine sulphate should not lose more than 12 per cent. of its weight. The official test with Rochelle salt and ammonia water depends upon the insolubility of cinchonidine tartrate, the tartrates of cinchonine and quinidine being dissolved and reprecipitated upon addition of ammonia.

Cinchonine Sulphate, $(C_{19}H_{22}ON_2)_2H_2SO_4 + 2H_2O$.—The usual process for making this salt is to dissolve the alkaloid cinchonine in warm diluted sulphuric acid until the acid is neutralized and then concentrate and crystallize the solution. The Pharmacopœia requires the absence of more than 5 per cent. of water of crystallization. Cinchonine sulphate may be readily distinguished from cinchonidine sulphate by its greater solubility in chloroform, 1 Gm. of the former requiring 47 mils. (or Cc.) for solution, while 1 Gm. of the latter requires 620 mils. (or Cc.) at 25° C. (77° F.).

Cocaine, $C_{17}H_{21}O_4N$ **or** $C_8H_{13}(C_6H_5CO)NO.COOCH_3$.—The leaves of Erythroxylon Coca contain a number of basic principles, all derivatives of ecgonine, $C_9H_{15}NO_3$, of which cocaine is the most important; other non-crystallizable bases are truxilline or isatropylcocaine (known also as cocamine), $C_{19}H_{23}NO_4$, hygrine, $C_{12}H_{13}N$, and cinnamylcocaine, $C_{19}H_{23}NO_4$. Cocaine appears in the plant united with coca-tannic

acid. The processes employed for the isolation of cocaine are usually guarded as secrets by manufacturers, and it is known that large quantities of the alkaloid are now prepared synthetically, owing to the difficulty of extracting *pure* cocaine in remunerative quantities from the drug.

When finely powdered coca leaves are moistened with solution of sodium hydroxide and then treated with petroleum ether, kerosene, or gasolin, the alkaloids present are liberated and taken up by the menstruum, from which they can be transferred, as salts, to diluted sulphuric acid, through intimate contact by agitation. If to this acid solution solution of sodium hydroxide be added in excess, cocaine mixed with some of the lesser alkaloids will be precipitated, the bulk of the hygrine, however, remaining in solution; the crude cocaine may be removed by filtration and expression and purified by crystallization from alcohol. As the yield of cocaine is known to decrease materially by transportation, no doubt owing to decomposition, the result of fermentation in the imperfectly dried and tightly packed leaves, much of the natural alkaloid is manufactured in South America, in places adjacent to the source of gathering the leaves, processes of extraction very similar to the above being employed. Large quantities of cocaine are made in this country.

In order to avoid loss of the decomposition products and other alkaloids accompanying cocaine in the crude article, the pure alkaloid is now extensively prepared by synthesis, in the following manner, which is possible, since the chemical constitution of cocaine is definitely known to be methyl-benzoyl-ecgonine. Boiling the mixed bases with hydrochloric acid converts them all into ecgonine, $C_9H_{15}NO_3$, and if ecgonine hydrochloride, $C_9H_{15}NO_3HCl$, be dissolved in methyl alcohol and the solution treated with dry hydrochloric acid gas, hydrochloride of methyl-ecgonine, $C_9H_{14}CH_3NO_3HCl$, will be formed and can be crystallized from an alcoholic solution. By heating this latter compound with benzoyl chloride, C_6H_5COCl. in a waterbath, until hydrochloric acid is no longer evolved and a homogeneous mass results, cocaine is obtained, which is freed from benzoic acid by solution in water, filtration, precipitation of the alkaloid with ammonia, and recrystallization from alcohol. Synthetic cocaine is identical in every respect with the natural alkaloid.

The purity of cocaine may be determined by its melting point, which is between 96° and 98° C. (204.8° and 208.4° F.), and after conversion into the hydrochloride by the tests given under that salt. The only use to which the alkaloid is put pharmaceutically is for the preparation of cocaine oleate, which is a 5 per cent. solution.

Cocaine Hydrochloride. $C_{17}H_{21}O_4N.HCl$.—This salt is prepared by dissolving the pure alkaloid cocaine in alcoholic solution of hydrochloric acid and crystallizing the anhydrous salt, which latter only is recognized in the Pharmacopœia.

The most important tests for the purity of the salt are the official tests with potassium permanganate, and with ammonia water, and Stockman's test with hot hydrochloric acid. By means of the first test it is intended to detect chiefly cinnamylcocaine, which is completely destroyed by potassium permanganate, whereas, in its absence, the pink color of cocaine permanganate remains permanent for thirty minutes and over. The test with ammonia water, also known as Maclagan's test, is intended to detect the presence of more than slight traces of isotropylcocaine, and depends upon the ready precipitation of cocaine alkaloid in crystalline form, when 0.2 mil. (or Cc.) of 10 per cent. ammonia water is added to 5 mils. (or Cc.) of a 2 per cent. solution of cocaine hydrochloride diluted with 80 mils. (or Cc.) of distilled water and the mixture actively stirred with a glass rod; if within 5 minutes crystalline cocaine does not separate, or if the solution upon the addition of ammonia water at once assumes a milky turbidity isotropylcocaine and other impurities are present. The presence of 0.5 per cent. of isotropylcocaine will prevent the formation of nearly all the precipitate and cause the liquid to be opalescent. If pure cocaine hydrochloride be carefully warmed in a test tube with about four times its weight of strong hydrochloric acid, until the mixture begins to boil, a colorless solution results; the degree of color, if there be any, is, in a measure, an indication of the amount of impurities present; the color thus obtained should never exceed that of a pale wine tint.

Other cocaine salts, such as the borate, citrate, lactate, nitrate, stearate, etc., have been put upon the market by manufacturing chemists, but their use is very limited.

Codeine. $C_{18}H_{21}O_3N + H_2O$ or $C_{17}H_{18}(CH_3)O_3N + H_2O$.—This alkaloid is obtained from opium, where it exists to the extent of 0.1 to 2 per cent. along with morphine, by treatment of an aqueous infusion of opium with chalk and calcium chloride, whereby codeine and morphine hydrochlorides are formed and can be purified by repeated crystallization. If a solution of these crystals be treated with ammonia, morphine will be precipitated, while codeine remains in solution and may be recovered by crystallization; if potassium or sodium hydroxide be used in place of ammonia, codeine will be precipitated, the morphine remaining in solution. Large quantities of codeine are now made synthetically from morphine by methylation, which is effected by allowing methyl iodide or chloride, or sodium methylsulphate, to act upon an alkaline solution of the latter alkaloid.

Codeine crystallizes from an aqueous solution with one molecule (5.67 per cent.) of water, which constitutes the official article; if crystallized from ether or carbon disulphide, it is anhydrous. Its crystals are larger than those of any other alkaloid and are soluble in about 120 parts of water.

Chemically, codeine is closely allied to morphine, as shown by the formula, $C_{17}H_{18}CH_3NO_3$, which differs from that of morphine by a methyl group, hence the name methyl-morphine. It differs, however, from morphine in its behavior toward certain reagents and may be readily distinguished from that alkaloid by the tests given in the Pharmacopœia. When heated with strong hydrochloric acid, in a sealed tube, both alkaloids yield apomorphine, but, if heated to 180° C. (356° F.) with a concentrated solution of zinc chloride, codeine yields *apocodeine*, $C_{18}H_{19}NO_2$, while morphine again yields apomorphine. The name codeine is derived from the Greek word χώδεια, meaning head, referring to the source of the alkaloid, poppy heads.

Codeine Phosphate, $C_{18}H_{21}O_3NH_3PO_4 + 2H_2O$.—This salt may be obtained by dissolving the alkaloid codeine in a mixture of phosphoric acid and water, and precipitating the newly formed compound by addition of alcohol; it may then be recrystallized after solution in hot water. The quantity of water of crystallization taken up by the salt is not uniform, thus, while the official salt of our Pharmacopœia contains 2 molecules or 8.32 per cent. of water, that of the British Pharmacopœia contains but 6.37 per cent.

Codeine phosphate is soluble in less than $2\frac{1}{2}$ times its weight of water, forming an acid solution. The Pharmacopœia requires that codeine phosphate shall yield not less than 67 per cent. of anhydrous codeine, if potassium hydroxide test-solution be added to an aqueous solution of an accurately weighed quantity of the salt and the mixture then shaken out with three or more successive portions of chloroform; the combined chloroform solutions are evaporated to dryness and dried to constant weight at 110° C. (230° F.).

Codeine Sulphate, $(C_{18}H_{21}O_3N)_2H_2SO_4 + 5H_2O$.—If codeine be dissolved in warm water, the solution exactly neutralized by addition of diluted sulphuric acid, and then concentrated by evaporation and set aside, codeine sulphate of the above composition, containing about 11.5 per cent. of water, will crystallize out. The salt contains about 76 per cent. of codeine and is far less soluble than codeine phosphate, but yields a neutral solution, requiring about 30 times its weight of water at 25° C. (77° F.).

Colchicine, $C_{22}H_{25}O_6N$ or $C_{15}H_{10}.(OCH_3)_3.NHCOCH_3.COOCH_2$.—Although colchicine was discovered in 1820, its true chemical nature was not determined until nearly seventy years later.

The pure alkaloid may be prepared by the following process, which is based upon the fact that it is capable of forming a crystalline compound with chloroform: Colchicum seed are exhausted with hot 90 per cent. alcohol, the alcohol recovered by distillation, the residue treated with water equal in quantity to $\frac{1}{5}$ of the weight of the drug used, and filtered for the removal of resin, wax, and fatty matter.

The clear, dark-brown, filtrate is well shaken with four successive portions of chloroform, which are united and distilled, the residue being again dissolved in water and shaken with chloroform. From the latter solution crude colchicine-chloroform separates upon evaporation of the solvent and is dissolved in alcohol, the solution being again concentrated by distillation. A third treatment with chloroform yields a yellow solution, which is evaporated on a waterbath, and the residue treated with lukewarm ether and set aside, when pure colchicine chloroform, having the composition $C_{22}H_{25}NO_6.2CHCl_3$, will separate in the form of faintly yellowish needle-shaped crystals, which are decomposed in the presence of water when heated to 100° C. (212° F.), the chloroform escaping and leaving pure colchicine in aqueous solution, from which it may be obtained as an amorphous mass by evaporation to dryness or in form of lamellæ by spreading the concentrated solution on plates of glass and drying.

Colchicine is more soluble in water than any other alkaloid, requiring but 22 parts at 25° C. (77° F.).

The salts of colchicine are not very stable. The one most used is the salicylate, $C_{22}H_{25}NO_6.HC_7H_5O_3$, made by moistening a mixture of 20 parts of colchicine and 7 parts of salicylic acid with water and subsequently drying the same. It is a yellow amorphous powder, soluble in water and alcohol.

Colchicine has on several occasions been found on the market contaminated by chloroform, due to imperfect preparation, and the Pharmacopœia gives a special test for its detection; if chloroform is present, the very disagreeable odor of phenyl isocyanide is developed when colchicine is heated with potassium hydroxide and aniline.

The name *colchisal* has been given to a solution of colchicine in methyl salicylate, dispensed in gelatin capsules, each containing 0.00025 Gm. of the alkaloid and 0.2 Gm. of the methyl ester.

Cotarnine Hydrochloride, also known as Cotarnine Chloride and Stypticin. $C_{12}H_{14}O_3NCl$ **or** $(CH_3O)(CH_2O_2).C_9H_6N(CH_3)Cl$.—Cotarnine may be obtained by boiling narcotine for some time with water, in which case cotarnine and meconin are formed, or by treating narcotine with oxidizing agents, when cotarnine and opianic acid result. The basic product is then treated with hydrochloric acid to obtain the official salt. It occurs as a yellow crystalline odorless powder, very soluble in water and in alcohol, producing yellow solutions.

Diacetylmorphine, also known as Heroine. $C_{17}H_{17}(C_2H_3O)_2O_3N$.—This synthetic alkaloid is obtained by heating pure morphine with acetyl chloride, washing the resulting product with dilute sodium carbonate solution and finally purifying it by crystallization from hot alcohol. It occurs as a white, crystalline, odorless powder, having a bitter taste; sparingly soluble in water, but readily soluble in alcohol

and in chloroform. The Pharmacopœia gives appropriate tests for the presence of morphine and foreign alkaloids.

Diacetylmorphine Hydrochloride, also known as Heroine Hydrochloride and **Diamorphine Hydrochloride.** $C_{17}H_{17}(C_2H_3O)_2O_3N.HCl + H_2O$.—This salt can be prepared by dissolving the free base diacetylmorphine in diluted hydrochloric acid, concentrating the solution and allowing it to crystallize. It resembles the free base in appearance, but is soluble in twice its weight of water and insoluble in chloroform.

Emetine Hydrochloride. $C_{30}H_{44}O_4N_2.2HCl$.—Since emetine is closely associated with cephaeline in ipecac, it becomes necessary to separate the two alkaloids carefully, which may be done by shaking an ethereal solution of the crude alkaloidal mixture obtained by precipitation of a concentrated alcoholic tincture of ipecac, with diluted sulphuric acid and then treating this acid solution with an excess of sodium hydroxide solution, whereby the emetine is precipitated while cephaeline remains in solution. The precipitated emetine is still further purified by washing and then dissolving it in diluted sulphuric acid; the acid solution being shaken out with ether in the presence of sodium hydroxide solution whereby any remaining cephaeline is removed. From the purified emetine thus obtained, the hydrochloride may be obtained by solution in diluted hydrochloric acid, concentration of the solution and crystallizing. Emetine is a diacid base, as shown by the formula of its hydrochloride.

Emetine hydrochloride occurs as a white or very slightly yellowish crystalline powder, odorless and gradually darkening on exposure to air; it is freely soluble in water and in alcohol. It crystallizes with variable amounts of water, the Pharmacopœia requiring, however, that when dried to constant weight at 100° C. (212° F.) it shall lose not more than 19 per cent. of its weight.

Ethylmorphine Hydrochloride, also known as Ethylmorphine Chloride, and Dionin. $C_{17}H_{17}O_2N(OC_2H_5)HCl + 2H_2O$.—If ethyl iodide be allowed to act on morphine dissolved in sodium or potassium hydroxide solution, ethylmorphine, $C_{17}H_{17}NOOHOC_2H_5$, is formed together with alkali iodide, the former being insoluble in the excess of alkali. The base may be purified by crystallization from hot alcohol, after which it is dissolved in hot water, neutralized with hydrochloric acid and the new salt obtained by crystallization. It occurs as a white or yellowish microcrystalline odorless powder, having a bitter taste, and soluble in 8 times its weight of water.

Homatropine Hydrobromide, $C_{16}H_{21}O_3NHBr$.—This salt, which resembles atropine in its physiological effects, is obtained by heating a concentrated neutral solution of tropine mandelate for several days on a waterbath with about half its volume of 12 per cent. hydro-

chloric acid. A part of the tropine mandelate remains intact and a part yields homatropine, which combines with the hydrochloric acid, forming a salt, which is subsequently decomposed with ammonia water and the liberated alkaloid extracted with chloroform. The chloroformic solution is freed from water with anhydrous potassium carbonate, and then distilled, yielding a syrupy liquid, which congeals to a crystalline mass, and may be exactly neutralized with diluted hydrobromic acid. The salt thus formed may be further purified by repeated crystallization from alcoholic solution. Homatropine hydrobromide may be distinguished from atropine, hyoscyamine and scopolamine by treating with fuming nitric acid, evaporating the mixture to dryness, and adding to the residue some freshly prepared alcoholic solution of potassium hydroxide, when homatropine gives a reddish-yellow color, while the other alkaloids cause a violet color. Another test depends upon the fact that while atropine and hyoscyamine hydrobromides are readily soluble in chloroform, the homatropine salt is very sparingly soluble in that liquid. The melting point of the pure alkaloid homatropine, obtained by precipitation with solution of sodium hydroxide and extraction with ether, is 19 degrees lower than that of atropine and 12 degrees lower than that of hyoscyamine, being only 96° C. (204.8° F.). The mydriatic effects of homatropine salts are of far shorter duration than those of atropine, and a solution instilled into the eye does not cause dryness of the throat and fauces, as in the case of atropine salts. The hydrochloride, sulphate, and salicylate of homatropine have also been used.

Hydrastine. $C_{21}H_{21}O_6N$.—This body must not be confounded with the mixture of resinoid substances sold under a similar name, hydrastin. The alkaloid, hydrastine, occurs in the root of hydrastis canadensis, golden seal, associated with berberine, and in commerce is frequently designated as the white alkaloid of hydrastis. Exactly how hydrastine exists in the drug was, for a long time, uncertain, some authorities contending that it is combined with an acid, and others that it exists free. According to investigations by Dohme and Engelhardt (1895), a portion of the alkaloid, about 20 per cent. of the total yield, exists in a free state, the remainder being in combination with an acid, the nature of which has not yet been determined. While formerly supposed to be present only in small proportions, hydrastine has been shown to occur frequently to the extent of 2.33 per cent. in the fresh or 3.14 per cent. in the dried root.

In extracting hydrastine for commercial purposes it becomes necessary first to remove the berberine. This is best done by adding a large excess of sulphuric acid to an alcoholic tincture of hydrastis root; after three or four hours a mass of crystals of berberine sulphate will have separated, and to the supernatant liquid, after filtration, ammonia water is added until the liquid is but slightly acid. Having removed the accumulated ammonium sulphate by straining, the liquid

is concentrated to a syrupy consistence and poured into ten times its bulk of cold water, whereby fat and resinous matter are precipitated. To the solution of crude hydrastine sulphate separated by filtration, ammonia water is then added in excess and the impure hydrastine collected, which may be purified by resolution in diluted sulphuric acid, reprecipitation by ammonia, and repeated crystallization from alcohol.

Hydrastine is a weak base, melting at 135° C. (275° F.), which, while readily soluble in acidulated water, forms difficultly crystallizable salts. It may be distinguished from hydrastinine by the blue fluorescence developed when a crystal of the alkaloid is dissolved in diluted sulphuric acid and a 10 per cent. solution of potassium permanganate then added. Hydrastine is extensively used in preparing the so-called "colorless hydrastis," which is a solution of the alkaloid in a mixture of water and glycerin with the aid of hydrochloric or sulphuric acid.

Hydrastine Hydrochloride, also known as Hydrastine Chloride. $C_{21}H_{21}O_6N.HCl$.—This salt may be prepared by dissolving the alkaloid hydrastine, reduced to powder, in a calculated quantity of diluted hydrochloric acid to form a neutral solution, concentrating the latter and allowing it to crystallize. It occurs as a white or creamy-white, crystalline, hygroscopic powder, which is odorless but has a bitter taste, and is freely soluble in water and in alcohol. Hydrastine hydrochloride may be easily distinguished from hydrastinine hydrochloride by the properties and tests mentioned under that salt.

Hydrastinine Hydrochloride, $C_{11}H_{11}O_2NHCl$.—The alkaloid hydrastinine does not occur in any plant, but is an artificial base obtained by oxidation of hydrastine—the white alkaloid found in hydrastine—by means of nitric acid. The mixture of hydrastine and nitric acid is moderately heated to 50° or 60° C. (122° to 140° F.) until ammonia water no longer causes precipitation. The reaction taking place produces hydrastinine and opianic acid, the latter crystallizing out on cooling of the solution, while hydrastinine is subsequently precipitated in crystalline form upon supersaturation of the filtrate with solution of potassium hydroxide.

Although hydrastinine hydrochloride is of light-yellowish or yellowish-white color, pure white alkaloid will separate after some time from a solution of 0.2 Gm. of the salt in 3 mils. (or Cc.) of water to which 4 or 5 drops of a 15 per cent. solution of sodium hydroxide have been added slowly, the mixture being shaken after each addition.

The salt is very soluble in water and alcohol; its aqueous solution, especially when highly diluted, shows a blue fluorescence and is not precipitated by addition of ammonia water, differing in this respect from the salts of hydrastine.

Hyoscyamine Hydrobromide, $C_{17}H_{23}O_3NHBr$.—The alkaloid hyoscyamine, discovered about 1833, is an isomer of atropine, being readily converted into the same, and is easily altered by alkalies and contact with heat, hence all manipulation and heating must be reduced to a minimum during its isolation. Hyoscyamine may be obtained from the mother-liquors left after the manufacture of atropine, or direct from henbane seed, as follows: Hyoscyamus seed having been freed from fatty matter by treatment with petroleum benzin and dried are exhausted with 85 per cent. alcohol. The tincture after acidulation with hydrochloric acid is concentrated in a vacuum apparatus and filtered, the filtrate being again treated with petroleum benzin and then rendered alkaline with potassium carbonate, after which it is shaken out with chloroform. Upon evaporation of the chloroformic solution at a low temperature, the hyoscyamine is obtained as a gummy mass and may be purified by solution in dilute sulphuric acid, filtering, and crystallizing. From the sulphate thus obtained, the alkaloid is liberated by making an aqueous solution alkaline and extracting with chloroform, which then yields hyoscyamine upon evaporation. Although crystallizable, hyoscyamine usually occurs in commerce in an amorphous condition. The exact relation between hyoscyamine and atropine was revealed in 1902 by Amenomiya, a Japanese chemist, who succeeded in converting atropine into dextro- and lævorotatory hyoscyamine; further details of this subject may be found in the *National Standard Dispensatory* 1916, p. 834.

Hyoscyamine hydrobromide may be prepared by dissolving 10 parts of the alkaloid in 11 parts of 25 per cent. hydrobromic acid, concentrating the solution, and crystallizing. It occurs in the form of white prismatic crystals without odor and, being deliquescent, should be preserved in tightly stoppered vials. It may be distinguished from atropine and scopolamine by forming minute lustrous golden-yellow scales of a double salt when treated with gold chloride test-solution as directed in the Pharmacopœia.

Morphine. $C_{17}H_{19}O_3N + H_2O$.—This is the most important of the large number of alkaloids found in opium, and, as before stated, was the first basic principle isolated from plants. It was called by its discoverer *morphium*, after the Greek deity *Μορφεύς*, the God of sleep, on account of its sleep-producing properties.

Morphine is present in opium in varying quantities, reaching as high as 12 or 14 per cent. in some samples of commercial opium not dried; the Pharmacopœia recognizes no opium yielding in its normal, moist condition less than 9.5 per cent. of anhydrous morphine, and demands not less than 10 per cent. nor more than 10.5 per cent. in the powdered article. It was formerly supposed to exist in combination with meconic acid only, but is now known to be present largely, if not altogether, as sulphate.

Morphine for commerce may be obtained in several ways; the natural salts being soluble in cold water, opium is exhausted with this menstruum, and the infusion, after concentration, treated either with sodium carbonate or with chalk and calcium chloride; the latter process is preferable, since meconic acid and coloring matters are precipitated as lime compounds, while the alkaloids are converted into soluble chlorides. After filtration the filtrate is concentrated, and yields a crystalline mass of morphine and codeine chlorides; narcotine remains in solution in the dark-colored mother-liquors; the crystals are purified by resolution in water, filtration through animal charcoal, and recrystallization. Finally, the mixed salts are dissolved in water and decomposed by addition of ammonia water, whereby the morphine is precipitated, the codeine remaining in solution. The morphine is subsequently recrystallized from hot alcohol. Other methods are known, and manufacturers, probably in each case, follow some favorite process.

The alkaloid morphine is rarely used in pharmacy, except in the preparation of the various oleates of morphine. The official article contains about 5.94 per cent. of water of crystallization, which it readily loses at 110° C. (230° F.), but parts with slowly at the temperature of a boiling waterbath; the Pharmacopœia demands that, when dried to constant weight at 100° C. (212° F.), it shall lose not more than 6.5 per cent. of its weight. Owing to the solubility of morphine in solutions of the fixed hydroxides and in lime water and insolubility in ether, as well as its characteristic reactions with oxidizing agents, it is readily distinguished from other alkaloids.

The permissible limit of foreign alkaloids in morphine is determined by solution of the alkaloid in sodium hydroxide solution, shaking out with successive portions of chloroform, evaporating the combined chloroform solutions to dryness, dissolving the residue in fiftieth-normal sulphuric acid and titrating the excess of acid with fiftieth-normal potassium hydroxide solution. Using 10 mils. (or Cc.) of fiftieth-normal acid for the residue obtained from 1 Gm. of morphine, not less than 7.5 mils. (or Cc.) shall be found uncombined, allowing 2.5 mils. (or Cc.) for neutralization of foreign alkaloids present.

Morphine Hydrochloride. $C_{17}H_{19}O_3NHCl + 3H_2O$.—By using diluted hydrochloric acid as a solvent for morphine alkaloid a solution of this salt is obtained which, upon concentration, yields well defined crystals containing 14.38 per cent. of water; an excess of acid should be avoided, as the salt is very stable and must have a neutral reaction. As made in this country, morphine hydrochloride occurs in large masses of feathery crystals, and is more bulky, weight for weight, than the sulphate. It can be rendered perfectly anhydrous at a temperature of 100° C. (212° F.), the Pharmacopœia not allowing more than 15 per cent. loss of weight, when so dried.

Morphine Sulphate. $(C_{17}H_{19}O_3N)_2H_2SO_4 + 5H_2O$.—Like the preceding salt, morphine sulphate is made by dissolving the alkaloid in sufficient diluted acid (sulphuric acid in this case) to form a neutral solution and after proper concentration allowing this to crystallize. The official salt contains 11.87 per cent. of water of crystallization, of which, however, only a part, 7.12 per cent. can be expelled at the temperature of a boiling waterbath.

Next to quinine sulphate there is probably no alkaloidal salt more extensively used by physicians than morphine sulphate, and unfortunately, owing to the lack of legal restrictions and the cupidity of some pharmacists and dealers in drugs, its unauthorized use among the laity for years led to much crime and misery by increasing the number of addicts to the opium habit. In recent years conditions have improved greatly, because of the better control of traffic in habit-forming drugs through the enforcement of both Federal and State laws, notably the Harrison Narcotic Law of 1914.

Pelletierine Tannate.—Under this title the Pharmacopœia recognizes a mixture in varying proportions of the tannates of four alkaloids obtained from the bark of pomegranate. The four alkaloids are pelletierine, isopelletierine, methylpelletierine, and pseudopelletierine, also known as punicine, isopunicine, methylpunicine, and pseudopunicine, the former names being preferred and given in honor of the French chemist, Pelletier.

To obtain the mixture of alkaloids designated as pelletierine tannate, the ground bark is mixed with milk of lime, transferred to a percolator, and exhausted with water. The resulting infusion is shaken out with chloroform, and the chloroformic solution of free alkaloids then shaken out with very dilute sulphuric acid. If to a neutral solution of the mixed sulphates a solution of tannic acid be added, the sparingly soluble tannates will be precipitated and are subsequently dried.

Commercial pelletierine tannate occurs as a light-yellow, odorless, amorphous powder, possessing an astringent taste and a weak acid reaction. It contains a small amount of moisture and requires about 240 parts of water or about 13 parts of alcohol for solution. Being a mixture of alkaloidal tannates, no formula can be given for its composition. Pure pelletierine, $C_8H_{15}NO$, which can be extracted from the above mixture, is a colorless, volatile liquid, having strong basic properties and forming crystallizable salts with acids. It is soluble in 23 parts of water and when exposed to air undergoes oxidation and turns dark.

Physostigmine Salicylate, also known as Eserine Salicylate, $C_{15}H_{21}O_2N_3C_7H_6O_3$.—The alkaloid physostigmine occurs in calabar beans to the extent of rarely more than one-sixth of 1 per cent., and its isolation requires considerable care, owing to its ready decomposition. The usual method of extraction is to exhaust the powdered bean with

85 per cent. alcohol and concentrate the tincture in a vacuum apparatus to a syrupy consistence; the resulting extract separates into an upper layer, consisting of fat, etc., and a lower, aqueous solution of the natural salts of the alkaloids. By treating the aqueous layer with sodium bicarbonate, and then repeatedly shaking with ether, the liberated physostigmine may be extracted; the ethereal solution is next treated with diluted sulphuric acid, so as to obtain a solution of the alkaloid as sulphate, leaving impurities, fat, resin, etc., in the ethereal liquid. The pure alkaloid is finally obtained by decomposing the sulphate with sodium bicarbonate, extracting again with ether and crystallizing. Heat must be avoided as far as possible, also the use of strong alkalies, as in the case of the mydriatic and other easily decomposable alkaloids.

Physostigmine salicylate may be prepared by neutralizing a solution of the alkaloid in absolute alcohol with pure salicylic acid; the salt gradually separates in colorless or faintly yellowish, shining needle-shaped crystals, which can be then drained and dried.

Some of the salts of physostigmine and their aqueous solutions readily assume a reddish color when exposed to light and air, hence they must be dispensed in tightly closed amber vials; the name rubereserine has been given to the red substance thus formed. The salicylate is less liable to change by exposure to light than the other salts; but, owing to its lesser solubility in water, is not as much used as the sulphate.

The name *eserine*, by which physostigmine is also known, was derived from the word *esère*, meaning split nut, the name applied by the African negroes to the calabar bean. Calabarine is the name given to another alkaloid present in the bean, which, however, is insoluble in ether.

Pilocarpine Hydrochloride, $C_{11}H_{16}O_2N_2HCl$.—The pure alkaloid pilocarpine is recognized in the French Pharmacopœia and may be obtained by moistening finely ground pilocarpus leaves with a solution of sodium carbonate and extracting with warm benzene. The benzene solution is shaken out with diluted hydrochloric acid, and after separation the acid liquid is made alkaline with sodium carbonate and shaken out with chloroform. Upon evaporation of the chloroformic liquids a mixture of crude alkaloids results, which is neutralized by means of nitric acid, evaporated to dryness, and purified by repeated crystallization from alcohol. Finally, the pilocarpine nitrate is dissolved in water, the solution made alkaline with ammonia water, and shaken out with chloroform; the latter solution, upon evaporation, yields the pure alkaloid in the form of a colorless, strongly basic, syrupy liquid, soluble in water, alcohol, and chloroform, but scarcely soluble in ether.

Pilocarpine hydrochloride is made by neutralizing diluted hydrochloric acid with pure pilocarpine, concentrating the solution and

setting the same aside to crystallize over sulphuric acid, or the solution may be evaporated to dryness, when the salt will be obtained as a crystalline powder. The salt is hygroscopic on exposure to air and when triturated with an equal weight of calomel forms a black mixture. The Pharmacopœia mentions the following special test as characteristic of the salts of pilocarpine: Dissolve 0.01 to 0.02 Gm. of the salts in 2 mils. (or Cc.) of water in a test tube, add 2 mils. (or Cc.) of a solution of hydrogen peroxide (slightly acid), and carefully pour on top of the liquid a small layer of benzene; then add 3 or 4 drops of a 0.3 per cent. solution of potassium dichromate and shake gently. The benzene layer will turn violet, while the aqueous layer will remain yellow. (If more than 0.02 Gm. is used, the benzene turns blue, and the reaction is no longer characteristic.)

The salts of pilocarpine are used chiefly as diaphoretics and sialogogues, but also possesses decided myotic properties, like those of physostigmine.

Pilocarpine Nitrate, $C_{11}H_{16}O_2N_2.HNO_3$.—This salt may be obtained as described above in the manufacture of pure pilocarpine, or by neutralizing diluted nitric acid with the pure alkaloid. After a neutral solution has been secured, the same is slowly evaporated to dryness, and the residue redissolved in hot alcohol and allowed to crystallize.

Pilocarpine nitrate differs from the hydrochloride in being permanent in the air and in not forming a black mixture when triturated with an equal weight of calomel. It responds to the special test mentioned in the preceding article.

Quinine. $C_{20}H_{24}O_2N_2 + 3H_2O$.—This is, no doubt, the most important and extensively used of all alkaloids. It occurs to a varying extent in the different species of cinchona, the yield having increased greatly with careful cultivation of the trees in India, Java, etc. The bases present in cinchona bark exist in combination with quinic or kinic, quinovic, and cinchotannic acids, and are usually extracted by means of acidulated water. The infusion is concentrated and mixed with milk of lime, whereby the alkaloids are liberated, while the calcium compounds of the organic acids are precipitated together with much coloring matter. By straining the mixture and exhausting the residue repeatedly with boiling alcohol, amyl alcohol, petroleum benzin, or kerosene, a solution of the crude alkaloids is obtained, from which the latter may be transferred as sulphates by treatment with diluted sulphuric acid. Another plan is to mix the powdered bark with solution of sodium hydroxide or milk of lime, whereby the natural combinations are broken up and the alkaloids liberated; the mixture is then exhausted, in a suitable apparatus, with hot alcohol or kerosene, from which, after proper concentration, the alkaloids are extracted as acid sulphates by means of sulphuric acid.

In either case the acid solution is treated with animal charcoal,

and the liquid, while hot, after filtration, is neutralized with solution of sodium hydroxide, when, upon cooling, neutral quinine sulphate crystallizes out and may be purified by resolution, recrystallization, etc. The other alkaloids, including also small quantities of quinine sulphate, remain in the mother-liquor and may be recovered as stated elsewhere.

From the purified quinine sulphate the alkaloid may be obtained by precipitation with sodium hydroxide, or ammonia water in very slight excess, after solution of the salt in water with the aid of an acid.

Official quinine alkaloid contains about 14.3 per cent. of water of crystallization, and melts at a comparatively low temperature, 57° C. (134.6° F.); at 100° C. (212° F.) about two-thirds of the water is expelled, but it does not become anhydrous until a temperature of 125° C. (257° F.) is reached. The Pharmacopœia states that, when dried to constant weight at 100° C. (212° F.) it loses not more than 15 per cent. of its weight. The commercial article varies considerably in appearance and solubility, due, no doubt, to different methods of manufacture; some is crumbly, compact, and idioelectric, dissolving slowly in alcohol and even dilute acids, while another lot is light, possesses no electric tendency, and dissolves readily.

The official test for the presence of appreciable quantities of other cinchona alkaloids depends upon the greater solubility of quinine alkaloid in ammonia water, and is carried out, after conversion of the alkaloid into quinine sulphate, as explained under Quinine Sulphate. A characteristic of the salt of quinine is the formation of a resin-like body, known as thalleioquin (from the Greek word θάλλός, thallos, meaning a green branch), recognized by the appearance of an emerald-green color when 1 or 2 drops of bromine test-solution are added to a dilute (1 per cent.) solution of the salt, followed by a slight excess of ammonia water. The thalleioquin reaction is also observed with the salts of quinidine, but these are not official and but little used; besides other reactions serve to distinguish quinidine from quinine.

Quinine and Urea Hydrochloride, also known as Quinine and Urea Chloride. $C_{20}H_{24}O_2N_2.HCl.CO(NH_2)_2.HCl + 5H_2O$.—This compound, which should contain not less than 58 per cent. of anhydrous quinine, may be prepared by dissolving quinine hydrochloride in diluted hydrochloric acid, adding the solution to pure urea, warming the mixture until solution has been effected, filtering through glass wool and setting the solution aside to crystallize. It occurs in colorless, translucent prisms or as a white granular powder, soluble in less than its own weight of water. Quinine and urea hydrochloride is admirably adapted for hypodermatic injection.

Quinine Bisulphate. $C_{20}H_{24}O_2N_2H_2SO_4 + 7H_2O$.—When neutral quinine sulphate is dissolved in water with the calculated necessary

quantity of sulphuric acid an acid salt will be formed, which can be obtained of the above composition by crystallization. Its solution in water shows a strong blue fluorescence and has a strong acid reaction. The salt contains a larger proportion of water of crystallization, 23 per cent., than other quinine salts, which it loses if heated to the temperature of boiling water; the Pharmacopœia requires that, when dried to constant weight, it shall lose not more than 25 per cent. of its weight. It is soluble at 25° C. (77° F.) in 9 parts of water, 18 parts of alcohol, or 18 parts of glycerin.

Quinine Dihydrochloride, also known as Acid Quinine Hydrochloride. $C_{20}H_{24}O_2N_2.2HCl$.—This salt may be made by decomposing a solution of quinine bisulphate with a solution of barium chloride, filtering the mixture and evaporating the filtrate to dryness at a temperature not exceeding 60° C. (140° F.), or by dissolving the official quinine hydrochloride in a mixture of water and hydrochloric acid and evaporating the solution to dryness. It occurs as a white, odorless powder, soluble in a little more than one-half its own weight of water, and is the most soluble of all quinine salts. The Pharmacopœia demands the absence of barium, as shown by the failure to produce turbidity if a few drops of diluted sulphuric acid be added to a 5 per cent. solution of the salt.

Quinine Hydrobromide, also known as Quinine Bromide, $C_{20}H_{24}O_2N_2HBr + H_2O$.—This salt can be made by dissolving the alkaloid quinine in warm diluted hydrobromic acid until neutralized and crystallizing the solution. It has also been obtained by double decomposition between an aqueous solution of potassium bromide and a warm alcoholic solution of quinine sulphate, the resulting potassium sulphate being precipitated, while the quinine hydrobromide is subsequently recovered by crystallization from a concentrated solution.

At the temperature of boiling water, quinine hydrobromide loses all its water of crystallization, 4.25 per cent. The salt is soluble at 25° C. (77° F.) in 40 parts of water, 0.67 part of alcohol, or 8 parts of glycerin. Its saturated aqueous solution does not show a blue fluorescence unless strongly acidulated with diluted sulphuric acid. The official test for the presence of other cinchona alkaloids involves the conversion of the quinine hydrobromide into quinine sulphate by interaction with sodium sulphate, after which the test is applied as in the case of quinine sulphate.

Quinine Hydrochloride, also known as Quinine Chloride. $C_{20}H_{24}O_2N_2HCl + 2H_2O$.—Like the preceding salt, quinine hydrochloride can also be made by double decomposition, but is usually obtained by dissolving the alkaloid quinine in sufficient diluted hydrochloric acid to form a neutral solution and allowing this to crystallize. The salt is soluble in 18 parts of water at 25° C. (77° F.); it is also soluble in

0.6 part of alcohol or 8 parts of glycerin. Moreover, like quinine hydrobromide it does not exhibit the usual blue fluorescence of quinine salts in concentrated solutions, unless acidulated with sulphuric acid; an excess of hydrochloric acid does not affect it. Commercially the salt is sometimes called muriate of quinine.

As in the case of quinine hydrobromide, this salt is converted into the sulphate by means of sodium sulphate before the test for the presence of other cinchona alkaloids is applied.

Quinine Salicylate. $C_{20}H_{24}O_2N_2.HC_7H_5O_3 + H_2O$.—This salt may be prepared by neutralizing an alcoholic solution of quinine with salicylic acid and allowing the solution, after concentration, to crystallize; it can also be obtained, as a curdy precipitate, by mutual decomposition between solutions of quinine hydrochloride and sodium salicylate, which can be dissolved in alcohol and crystallized in an anhydrous state.

Quinine salicylate contains 3.75 per cent. of water of crystallization, and is soluble in 77 parts of water, 11 parts of alcohol, or 16 parts of glycerin.

In the official test for the presence of other cinchona alkaloids, the salt is first decomposed with ammonia water and the quinine extracted with ether; the latter is then dissolved in diluted sulphuric acid, and the resulting quinine sulphate recovered by evaporation. After this the test with ammonia water may be applied under the same conditions as stated under Quinine Sulphate.

Quinine Sulphate. $(C_{20}H_{24}O_2N_2)_2H_2SO_4 + 7H_2O$.—The official salt is the neutral sulphate, although termed by some basic sulphate; it is also known as quinine disulphate, but this term is incorrect and should not be used, diquinine sulphate indicating the true chemical composition. The manufacture of this most important alkaloidal salt has already been explained in connection with the preparation of quinine alkaloid. In order to insure a large yield of the salt it is necessary that the hot solution from which it is to crystallize be of a neutral reaction; the sulphates of the other alkaloids present are all far more soluble in cold water than quinine sulphate, and will, therefore, almost wholly remain in the mother-liquors. Small quantities of the lesser alkaloids are no doubt always present in the commercial article, but should not be detectable by the official test with ammonia water; the United States Pharmacopœia fixes no percentage limit of impurities.

The official test with ammonia water for other cinchona alkaloids known as Kerner's test, depends upon the greater solubility of the sulphates of the other cinchona alkaloids in cold water and the greater solubility of quinine alkaloid in ammonia water. The test must be carried out with care as the amount of ammonia water necessary to produce a clear liquid depends upon the maintenance of a definite temperature during maceration of the dried quinine sulphate with

water; the Pharmacopœia prescribes 15° C. (59° F.), in which case 7 mils. (or Cc.) of 10 per cent. ammonia water must suffice for the 5 mils. (or Cc.) of filtrate used in the official test. If the temperature during maceration has been 16° C. (60.8° F.), 7.5 mils. (or Cc.) of ammonia water may be added, and if 17° C. (62.6° F.), 8 mils. (or Cc.) may be added. The reason for this increased quantity of ammonia water is that, naturally at a higher temperature more quinine sulphate will be dissolved and consequently more ammonia water will be necessary to produce a clear liquid.

De Vrij and Schaefer have shown that a considerable percentage of lesser cinchona alkaloids may escape detection by Kerner's test; hence the German Pharmacopœia has adopted a modification by Kerner and Weller, which consists in digesting in a test tube 2 Gms. of quinine sulphate dried at 40° or 50° C. (104° or 122° F.) with 20 mils. (or Cc.) of distilled water at 60° or 65° C. (140° or 149° F.) for 30 minutes, with frequent agitation. The tube and contents are then cooled and kept at a temperature of 15° C. (59° F.) for two hours, with frequent agitation, after which the mixture is filtered; 5 mils. (or Cc.) of the filtrate should yield a clear solution with 4 mils. (or Cc.) of 10 per cent. ammonia water. This test is much more severe than that of the United States Pharmacopœia, and demands a much purer salt. Whenever solutions of alkaloidal salts are filtered it should be borne in mind that filter paper abstracts appreciable quantities of the salt from solution; it should, therefore, either be filtered through glass wool, or the filtrate through paper should be collected in fractions of 5 mils (or Cc.) each, of which the second or third fraction only should be used for the above test.

Quinine sulphate can be crystallized with varying proportions of water, the official salt being allowed as much as 16.2 per cent. As the salt effloresces upon exposure, the symbolic formula given in the Pharmacopœia representing 14.43 + per cent. of water probably indicates the average composition of the commercial salt. Very appreciable loss of weight has been observed in cases where the salt was preserved in paper boxes, hence manufacturers use either glass or tightly sealed tin containers. It is the least soluble of the official quinine salts, requiring at 25° C. (77° F.) 720 parts of water, or 86 parts of alcohol, or 36 parts of glycerin. At 60° C. (140° F.) it loses all but 2 molecules of its water of crystallization, the remainder not being entirely expelled until a temperature of 115° C. (239° F.) is reached.

Quinine Tannate.—This official compound of quinine and tannic acid is of somewhat varying composition and hence no definite chemical formula can be given for the same. It may be prepared by the method given in the German Pharmacopœia, which directs that 2 parts of quinine sulphate be dissolved in 60 parts of water with the aid of the least possible quantity of diluted sulphuric acid; to this solution is

added a solution of 4 parts of tannic acid in 25 parts of water, in small portions, followed by a solution of 1 part of tannic acid in 16 parts of water and 1 part of ammonia water, constantly stirring the mixture. The resulting precipitate is allowed to subside for 12 hours, collected, washed with water, expressed and warmed with 10 parts of water until a translucent, yellowish-brown, resinous mass is obtained, which is dried at 30° to 40° C. (86° to 104° F.) and finally at 100° C. (212° F.) and reduced to powder.

Quinine tannate occurs as a pale yellow or yellowish-white amorphous, odorless and almost tasteless powder, which is slightly soluble in water. The Pharmacopœia requires that it shall contain not less than 30 per cent. nor more than 35 per cent. of anhydrous quinine, and when dried to constant weight at 100° C. (212° F.) shall not lose more than 10 per cent. of its weight. The presence of uncombined quinine may be determined by extraction with anhydrous ether, and should not exceed 0.5 per cent. The combined quinine is determined in a similar manner, after treatment of a mixture of the compound and water with ammonia water.

Scopolamine Hydrobromide, also known as Scopolamine Bromide and Hyoscine Hydrobromide. $C_{17}H_{21}O_4N.HBr + 3H_2O$.—The alkaloid scopolamine (or hyoscine), although occurring in several plants, is obtained chiefly from the seed of hyoscyamus and stramonium, either by neutralizing the mother-liquors remaining after the removal of hyoscyamine, with hydrobromic acid and adding absolute alcohol, when after the lapse of some time crystals of scopolamine hydrobromide will separate and may be purified by recrystallization from hot alcohol, or by obtaining pure scopolamine from a purified double salt of the alkaloid and gold and dissolving this in diluted hydrobromic acid and allowing the solution to crystallize.

Scopolamine hydrobromide contains about 12.33 per cent. of water of crystallization and the Pharmacopœia requires that, when dried to constant weight at 100° C. (212° F.) it shall not lose more than 13 per cent. of its weight. The two names scopolamine hydrobromide and hyoscine hydrobromide are interchangeable, both referring to the same salt.

Sparteine Sulphate. $C_{15}H_{26}N_2H_2SO_4 + 5H_2O$.—Sparteine is the only alkaloid belonging to the class of amines recognized in the Pharmacopœia. It is a liquid heavier than water, and has been obtained by extracting scoparius with water acidulated with sulphuric acid, concentrating the infusion, decomposing the salt with sodium hydroxide, and distilling. The distillate is supersaturated with hydrochloric acid, evaporated to dryness, and distilled with the aid of potassium hydroxide; first ammonia passes over, after which sparteine distils and condenses as a thick, oily liquid. Another method consists in exhausting the powdered drug with 60 per cent. alcohol, evaporating

the tincture at a low temperature, and extracting the alkaloid with the aid of tartaric acid; the solution of sparteine tartrate is then decomposed with potassium carbonate, and the alkaloid thus liberated abstracted with ether. Pure sparteine is a colorless fluid, boiling at 287° C. (548.6° F.), and having an aniline-like odor and intensely bitter taste. It is easily decomposed upon exposure to air and light.

Sparteine sulphate is prepared by neutralizing the purified alkaloid with diluted sulphuric acid and rapidly concentrating the solution, when colorless crystals will be obtained. As indicated by the official formula, it is the salt of a diacid base. The Pharmacopœia recognizes the presence of 5 molecules (21.34 per cent.) of water of crystallization, which compound is obtained by recrystallizing the salt from diluted alcohol. Sparteine sulphate crystallizes with different proportions of water under varying conditions, and also occurs in the form of an anhydrous salt. It is hygroscopic and is soluble in a little more than its own weight of water, yielding a solution having an acid reaction toward litmus.

Strychnine. $C_{21}H_{22}O_2N_2$.—This alkaloid occurs in combination with an acid to which formerly the name igasuric acid was given, but which has been shown to be a variety of tannic acid, similar to caffeotannic acid. It is generally associated with brucine, in the seed of strychnos nux vomica and other members of the natural order Loganiacæ. The proportion of strychnine present in the seed varies, sometimes reaching as high as 1.8 per cent.

To extract the alkaloids the powdered drug may be exhausted with boiling water acidulated with hydrochloric or sulphuric acid, whereby the alkaloids are obtained in solution as hydrochlorides or sulphates. Upon concentration of the infusion and addition of milk of lime the alkaloids are precipitated, and by collecting upon a strainer and washing the residue with water much foreign matter is removed. Subsequent treatment of the residue with cold diluted alcohol removes brucine, the treatment being continued as long as the washings are reddened by nitric acid, after which boiling alcohol is used to extract the strychnine; this, after recovery of the alcohol, is converted into sulphate by solution is diluted sulphuric acid, filtered through animal charcoal, and precipitated with an alkali.

Some manufacturers exhaust the drug with hot alcohol of about 60 per cent., concentrate the tincture, filter, and add lead acetate, whereby the tannic acid is removed together with coloring matter, while the alkaloids remain in solution as acetates. After a second filtration the alkaloids are precipitated by ammonia, and may be further treated as above or dissolved in hot alcohol, from which the strychnine will crystallize on cooling, and may be freed from adhering brucine by washing with diluted alcohol.

Commercial strychnine occurs both in the form of crystals and powder, the latter being preferred for dispensing purposes. Its taste

is so intensely bitter that it is perceptible if but $\frac{1}{8}$ grain be dissolved in 10 gallons of water.

The blue color obtained when strychnine is added to a solution of potassium dichromate and sulphuric acid is due to an oxidation product, the exact nature of which is unknown, as it has not been possible to isolate the blue compound on account of its evanescent character.

Strychnine Nitrate. $C_{21}H_{22}O_2N_2.HNO_3$.—This salt may be obtained by dissolving a convenient quantity of strychnine in sufficient diluted nitric acid to form a neutral solution, which is then concentrated and allowed to crystallize. It is permanent in the air and somewhat less soluble in water than strychnine sulphate, requiring about 42 parts for solution at ordinary room temperature. The salt should be free from brucine and correspond to all the characteristic tests for strychnine. It contains a little over 84 per cent. of strychnine, and is therefore relatively nearly 10 per cent. stronger than the sulphate.

Strychnine Sulphate. $(C_{21}H_{22}O_2N_2)_2H_2SO_4 + 5H_2O$.—This salt is best prepared by dissolving the alkaloid strychnine in warm diluted sulphuric acid, avoiding an excess of the latter; if a hot saturated solution is obtained, the salt will crystallize with 5 molecules (about 10.5 per cent.) of water, as required by the Pharmacopœia. When exposed to dry air the salt effloresces, and when heated to the temperature of boiling water loses all of its water of crystallization. It contains very nearly 78 per cent. of strychnine, and should be soluble in 32 parts of water at 25° C. (77° F.); the solubility is influenced by a possible loss of water of crystallization, and hence the salt must be preserved in tightly closed vials.

Theobromine Sodio-salicylate.—This preparation, also known as diuretin, is a mixture of sodium theobromine and sodium salicylate in approximately molecular proportions. It may be made by dissolving theobromine in a strong solution of sodium hydroxide with the aid of waterbath heat, adding to the solution of sodium theobromine thus obtained a solution of sodium salicylate, filtering the liquid if necessary, and evaporating to dryness on a waterbath.

It occurs as a white, odorless powder having a sweetish saline and somewhat alkaline taste, soluble in its own weight of water, but becoming partially insoluble by exposure to air, owing to absorption of carbon dioxide and liberation of theobromine.

The Pharmacopœia requires that theobromine sodio-salicylate, when dried to constant weight in a desiccator over sulphuric acid, shall yield not less than 46.5 per cent. of theobromine, and gives a method for its determination. The possible presence of caffeine in the mixture is limited to $\frac{1}{2}$ per cent.

Theophylline. $C_7H_8O_2N_4 + H_2O$ or $C_6H_2(CH_3)_2O_2N_4 + H_2O$.—Although the alkaloid theophylline occurs in the leaves of the tea plant, it is present in such small quantity that its extraction would not prove successful commercially, and no doubt all now on the market is produced synthetically by patented processes, which are rather complicated. While theophylline is isomeric with theobromine, both being known as dimethylxanthine, the two alkaloids differ in constitution, theophylline being 1 : 3 dimethylxanthine and theobromine 3 : 7 dimethylxanthine, that is, the methyl groups occupy different positions in the molecule.

Theophylline occurs as a white, odorless crystalline powder, soluble in 100 times its weight of water, but more soluble in alcohol and in hot water. It may be distinguished from caffeine and theobromine by yielding a clear solution with 25 times its weight of ammonia water or sodium hydroxide test-solution; like caffeine and theobromine, however, it forms tetramethyl murexide, $C_8(CH_3)_4O_6N_5(NH_4)$, of a rich purple color, when treated with hydrochloric acid and potassium chlorate and finally exposed to the fumes of ammonia water (see under Caffeine on p. 816). A saturated aqueous solution of theophylline shows a neutral reaction with litmus.

Synthetic theophylline is the first instance of the successful production of an alkaloid on a commercial scale by strictly artificial methods. The name *theocin* has been applied by one of the manufacturing firms to its synthetic product to distinguish it from that of other firms and also from the natural alkaloid.

Veratrine.—The substance recognized, both in the Pharmacopœia and commercially, by the name veratrine is a mixture of alkaloids obtained from cevadilla seed. The mixture of alkaloids in the seed being very complex, no attempt is made at separation in the process of extraction. The seed, having been crushed, are exhausted by repeated boiling with acidulated water and the mixed decoctions evaporated to a syrupy consistence and treated with milk of lime. The precipitate thus obtained by decomposition of the natural salts of the alkaloids with veratric acid, and consisting of crude alkaloids and extractive matter, is extracted with alcohol and the latter recovered from the resulting solution, after which the residue is digested with acetic acid in order to bring the alkaloids into solution as acetates. The last named solution is decomposed with ammonia water in excess and the precipitate, having been washed with water, is dissolved in diluted hydrochloric or sulphuric acid, the solution decolorized with animal charcoal and again precipitated with an alkali. Finally, the precipitate of mixed alkaloids is washed with water and dried at moderate temperature. This process has the advantage over others in avoiding the extraction of fatty and resinous matter.

The most abundant and most important alkaloid in veratrine is cevadine, $C_{32}H_{49}O_9N$, which may be crystallized from alcohol in the

form of anhydrous needles. It is exceedingly toxic and very irritating to the nasal mucous membrane. A solution of cevadine in nitric acid assumes a violet color upon being warmed, which changes to scarlet-red on boiling. With cold sulphuric acid cevadine yields a yellow solution, the color, however, changing to blood-red on warming. According to Allen, the facility with which cevadine undergoes hydrolysis is the cause of the formation of much amorphous alkaloid and other products in the extraction of cevadilla seed.

Besides cevadine, veratridine, $C_{37}H_{53}O_{11}N$, named veratrine by its discoverers, Luff and Wright, is present in the official veratrine, and also cevadilline or sabadilline, $C_{34}H_{53}O_8N$, both of which are amorphous. Sabadine, $C_{29}H_{52}O_8N$, and sabadinine, $C_{37}H_{48}O_8N$, both crystallizable alkaloids, have also been found.

Owing to its intensely irritating effect upon the mucous membranes, care is necessary in handling veratrine, and dampening with alcohol or expressed oil of almond will be found desirable when mixing it with other substances. Veratrine is rarely used internally, but mostly as oleate or liniment.

Veratrine is not found in white or green hellebore, but other alkaloids, *jervine*, $C_{26}H_{37}O_3N$, and *veratroidine*, $C_{51}H_{78}O_{16}N_2$, have been isolated from these plants.

Besides the foregoing there are a number of alkaloids and alkaloidal salts not recognized in the Pharmacopœia which are of more or less interest to pharmacists, and will, therefore, be briefly considered.

Arecoline Hydrobromide. $C_5H_{13}O_2NHBr$.—This salt, which is official in the German Pharmacopœia, may be obtained by dissolving the pure alkaloid in diluted hydrobromic acid and crystallizing from an alcoholic solution. The alkaloid arecoline occurs in the areca or betel nut to the extent of 0.1 per cent., and its extraction involves a tedious and somewhat complicated process; it is the only one of the four alkaloids found in the areca nut which is highly poisonous, and, while an oily liquid of strongly basic reaction, it is soluble in water in all proportions.

Berberine. $C_{25}H_{17}O_4N$.—The chief interest attached to this alkaloid arises from the fact that, while the alkaloid is soluble in water, its salts are difficultly soluble, and are deposited in a crystalline form from acid liquids. Berberine occurs in several plants—in hydrastis to the extent of 3 or 4 per cent., from which it may be obtained by adding to a concentrated aqueous infusion of the drug, hydrochloric or sulphuric acid in excess, when the corresponding berberine salt will be deposited in crystals, which, after purification by recrystallization from boiling water, may be decomposed by means of freshly prepared lead hydroxide. After filtration and concentration of the filtrate, berberine will separate as a yellow, crystalline powder.

Narcotine. $C_{22}H_{23}O_7N$.—This substance occurs in opium, sometimes to the extent of 10 per cent. and over. Being readily soluble in chloroform and ether, it is easily extracted from powdered opium by maceration or percolation with either of these solvents, but, not being soluble in petroleum benzin, it is not removed in the present official processes for Deodorized Opium and Tincture of Deodorized Opium. Narcotine is a very weak base and does not neutralize acids; it exists in opium in a free state, and, although it forms crystallizable compounds with hydrochloric and sulphuric acids, these are readily decomposed by an excess of water, and yield narcotine to both ether and chloroform when shaken with these liquids. A solution of narcotine in sulphuric acid soon becomes yellow, and, upon heating, turns red, and finally purple.

Quinidine Sulphate. $(C_{20}H_{24}O_2N_2)_2H_2SO_4 + 2H_2O$.—Quinidine usually remains in the mother-liquors from the crystallization of quinine sulphate, from which it may be obtained by adding a large excess of ammonia water, whereby cinchonine and cinchonidine are thrown down, while quinidine remains in solution; it can subsequently be precipitated by means of caustic soda and dissolved in diluted sulphuric acid, the resulting salt being purified by recrystallization. From the purified alkaloid, obtained by precipitation with sodium hydroxide, the sulphate can be readily prepared by solution in just sufficient warm diluted sulphuric acid to neutralize the same and crystallizing.

Quinidine sulphate somewhat resembles official quinine sulphate in appearance, and has some chemical properties in common with it, but may be distinguished by its greater solubility in water and in alcohol and by being precipitated in concentrated aqueous solution by potassium iodide. Its solutions, like those of quinine sulphate, form thalleioquin and show a blue fluorescence when acidulated with sulphuric acid.

The alkaloid quinidine is used in making the so-called Bitterless Syrup of Quinidine recognized in the *National Formulary* as Syrup of Quinidine, which contains 0.033 Gm. of the alkaloid in each mil. (or Cc.) or about 2 grains in each fluidrachm.

CHAPTER LXI.

ASSAY OF ALKALOIDAL DRUGS.

In view of the fact that the Pharmacopœia demands a definite alkaloid content for a large number of crude drugs and galenical preparations, a discussion of the subject appears desirable for the purpose of offering to students some explanation of the official and other methods in use for the quantitative determination of active principles. In the case of alkaloidal drugs the valuation may be made either gravimetrically or volumetrically, but with accuracy only if a single alkaloid is present, or if the exact proportion of the several alkaloids present be known, or if the percentage of total alkaloids only is desired.

The assay of alkaloidal drugs by what is known as the "shaking out process," for which the Pharmacopœia gives general directions on pages 594 and 595, depends on the solubility of uncombined alkaloids in ether, chloroform, petroleum benzin and similar liquids, and the general insolubility of their salts in these solvents. Hence, by the use of immiscible solvents, it is possible to purify the alkaloidal constituents of a drug by alternately transferring them from the condition of a salt to that of a free alkaloid and vice versa; in this way coloring matters, fats and resins may be gotten rid of almost entirely.

The first step in assaying alkaloidal drugs is to extract them with ether or chloroform, or a mixture of these two liquids, in the presence of an alkali, usually ammonia water. As a rule 10 or 15 Gms. of the drug in powder form, not coarser than No. 40 and preferably finer, is treated with 100 or 150 mils. (or Cc.) of the solvent, and after due maceration (from 1 to 4 hours), with frequent agitation, an aliquot part of the fluid is withdrawn, representing a definite weight (5 or 10 Gms.) of the drug. As it is often difficult to pour off an aliquot part of the lighter liquid entirely free from floating particles, distilled water is added to the mixture (from 10 to 30 mils. (or Cc.) as may be necessary) just before the liquid is to be poured off, and the mixture actively shaken for a few minutes; this causes the powdered drug to ball together and settle, and permits the separation of a perfectly clear upper layer, easily removed by decantation.

The decanted alkaline solution is then shaken out in a separator with successive portions of diluted sulphuric or hydrochloric acid, using for the first extraction half-normal acid and for subsequent extractions a mixture of equal volumes of half-normal acid and distilled water, whereby the alkaloids are removed as salts in aqueous solution. In all assays the extraction with acid should be continued until 0.5 mil. (or Cc.) of the acid washings shows barely a faint cloudi-

ness on the addition of 1 drop of Mayer's Solution (see below), or in the case of caffeine and colchicine, on the addition of a drop of iodine test-solution. The combined acid solutions are transferred to another separator, made alkaline by addition of an excess of ammonia water, or solution of potassium or sodium hydroxide, and shaken out with successive portions of ether or chloroform until all alkaloid has been removed. The combined ether or chloroform solutions are then carefully evaporated to dryness and weighed or titrated as may be directed in the individual case.

When fluidextracts and tinctures of alkaloidal drugs are to be assayed, it has been found advantageous in some cases to distribute these liquids (the tinctures after concentration to a small bulk) over purified sawdust,[1] which is then dried at a moderate temperature before treating it with ether and ammonia water, or with chloroform, ether and ammonia water, as in the case of the crude drug. From this point the assay process is the same as outlined above for the powdered drug.

In the case of pilular extracts to be assayed, these are usually dissolved in a small quantity of diluted alcohol, transferred to a separator and after the addition of ammonia water, shaken out with ether or a mixture of chloroform and ether; the alkaline solution is then further treated as stated above for the assay of crude drugs. Powdered extracts are preferably thoroughly mixed with about five times their weight of washed sand, transferred to a flask or vial, and after the addition of ammonia water and ether or chloroform and ether, vigorously shaken every few minutes during a half hour; when the dregs have settled, an aliquot part of the clear liquid is decanted and transferred to a separator, to be further treated as in the case of pilular extracts.

Some alkaloids, especially those of aconite and the mydriatic drugs are very sensitive to heat, either alone or in the presence of strong alkalies, and hence a moderate temperature, not exceeding 50° C. (122° F.) should be employed for the final evaporation of the ether or chloroform solutions. In some cases the use of potassium carbonate or sodium bicarbonate is also decidedly preferable to that of the caustic alkalies.

If the determination of alkaloidal content is to be made gravimetrically, the weight of residue obtained by evaporation, as stated above, should, in the case of crude drugs, pilular and powdered extracts, be multiplied by 100 and divided by the weight of the drug or extract

[1] The Pharmacopœia directs the purified sawdust for assay work to be prepared as follows: One thousand Gms. of oak sawdust, in about No. 20 powder, is moistened with water, packed in a cylindrical glass percolator and saturated with sufficient 1 per cent. sodium hydroxide solution to leave a stratum above the mass. When the liquid begins to drop from the percolator, close the lower orifice and macerate the sawdust for 24 hours. Then allow percolation to proceed slowly until the alkaline percolate measures 5000 mils. (or Cc.). Continue percolation with 4000 mils. (or Cc.) of 1 per cent. hydrochloric acid, and then with water until the acid has all been removed and the percolate is neutral. Finally dry the purified powder.

represented in the final solution which will express the percentage of alkaloid present in the sample. In the case of fluidextracts and tinctures, the method of calculation must be slightly changed in order to conform to the official requirements, thus: the weight of alkaloid obtained should be multiplied by 100 and divided by the number of mils. (or Cc.) of fluidextract or tincture represented in the final alkaline solution in order to ascertain the weight of alkaloid in 100 mils. (or Cc.).

As a rule the alkaloidal residue obtained is more or less contaminated with coloring matter and other impurities, and hence the weight found gives results that are too high; for this reason the gravimetric method of assay is confined to those drugs in which it is possible to obtain the alkaloid in a pure state, preferably in crystal form, as for instance in the case of such drugs as cinchona, coca, colchicum, guarana, hydrastis, and opium.

If a volumetric determination is to be made, the residue of crude alkaloid is dissolved in a measured quantity of tenth-normal acid, with the aid of moderate heat if necessary, sufficient acid being used to insure an excess, which latter is then determined by titration with fiftieth-normal alkali in the presence of a suitable indicator, either hematoxylin, cochineal, methyl red, or iodeosin solution, the latter being especially intended for colored alkaloidal residues. The object of using alkali solution so much weaker than the acid is to enable the operator to approach the end of the reaction with greater precision, avoiding a large excess of alkali, and the quantity of such weaker alkali solutions used must be brought to the equivalent of the stronger acid solution by calculation. Thus, if fiftieth-normal alkali is used, 5 mils. (or Cc.) will be equivalent to 1 mil. (or Cc.) of tenth-normal acid, and hence the number of mils. (or Cc.) necessary to neutralize the acid must be divided by 5 to find the exact number of mils. (or Cc.) of tenth-normal acid in excess, and if this number be subtracted from the quantity of acid originally used the difference will indicate the quantity of acid neutralized by the alkaloids. Having ascertained the number of mils. (or Cc.) of tenth-normal acid taken up by the alkaloids, the same is multiplied by the factor representing the weight of the respective pure alkaloids equivalent to 1 mil. (or Cc.) to find the total quantity of alkaloid in the residue, from which the percentage of alkaloid present in the sample of drug is readily calculated as shown above.

The following list indicates the quantity of some of the leading alkaloids (anhydrous) necessary to neutralize 1 mil. (or Cc.) of tenth-normal acid:

Aconitine,	0.064539 Gm.	Emetine,	0.024718 Gm.
Atropine,	0.028919 "	Hydrastine,	0.038318 "
Cephaeline,	0.023316 "	Morphine,	0.028516 "
Cinchonidine,	0.029420 "	Phytostigmine,	0.027520 "
Cinchonine,	0.029420 "	Pilocarpine,	0.020815 "
Cocaine,	0.030318 "	Quinine,	0.032421 "
Coniine,	0.012715 "	Strychnine,	0.033420 "

An annoying feature sometimes encountered in the shaking-out process of alkaloidal solutions is the formation of persistent emulsions, which is usually caused by too active agitation of the contents of the separator. It may be avoided, in a large measure, by inverting the separator several times and then carefully rotating the same, without agitation, so as to cause successive fresh surfaces of the immiscible liquids to be intimately ground together, whereby the alkaloids will be transferred perfectly from one liquid to another. The use of a large volume of chloroform or ether, as the case may be, in proportion to the volume of aqueous fluid, also tends to prevent the formation of emulsions. If an emulsion has been formed, several plans may be tried to cause separation, as follows: If the alkaloidal solvent is heavier than water, more of the solvent and a small quantity of water should be added; and if the solvent be lighter than water, sufficient sodium chloride solution may be added to cause separation. As heat is detrimental to the permanency of emulsions the application of a cloth, preferably flannel, dipped in hot water to the outside of the separator has been found quite effectual in many cases. The use of powdered tragacanth has been recommended for breaking emulsions of immiscible solvents and is said to work admirably by abstracting the water; a quantity of the powder is added to the emulsion and the separator then vigorously shaken for a few moments, when the tragacanth will form a lump or ball with the water and the ether or chloroform can then be readily decanted or withdrawn. When the emulsion is not large in quantity, a very simple device is to place a pledget of absorbent cotton well up in the tube of the separator and filter the emulsion through the same; this works well especially in the case of chloroform emulsions. Slight emulsions are usually broken up if a glass rod be introduced as far as the bottom of the emulsion and then repeatedly twirled and slowly drawn upward.

In every case of alkaloidal determination the operator must convince himself that all the alkaloid present in the sample has been extracted and that none be lost during the several steps of the process; this is best done by means of Mayer's Solution (official mercuric potassium iodide test-solution), which produces with acid solutions of the alkaloids a cloudiness or precipitate, depending on the amount of alkaloid present. When this test is applied all alcohol, chloroform, or ether must be removed from the liquid before Mayer's Solution is added, otherwise the reaction will not be visible on account of the solvent effect of the substances named. The proper mode of procedure is to place a small quantity of the liquid to be tested, 0.5 or 1 mil. (or Cc.) in a test tube or glass dish, and, if alkaline, make acid by the addition of sufficient dilute sulphuric acid; then warm gently to drive off any alcohol or chloroform and add 2 or 3 drops of the reagent. If no cloudiness appears upon holding the tube or dish against a dark background all traces of alkaloid are absent. The test should be applied particularly when transferring alkaloids in

separators from one liquid to another, as from an alkaline to an acid fluid, or vice versa, in the shaking-out process. Mayer's Solution is, however, not suitable in all cases and for determining the complete removal of caffeine or colchicine, the Pharmacopœia directs the use of iodine test-solution instead; it is used in the same manner as the solution of potassium mercuric iodide.

For the convenience of students the official methods for the assay of drugs and their preparations are here given, together with such comments as may seem desirable.

ASSAY OF ACONITE AND ITS PREPARATIONS.

The Pharmacopœia requires that when tested by the official method of assay, given below, aconite shall yield not less than 0.5 per cent. of the ether-soluble alkaloids of aconite; extract of aconite, not less than 1.8 per cent. nor more than 2.2 per cent.; fluidextract of aconite, not less than 0.45 Gm. nor more than 0.55 Gm. in 100 mils. (or Cc.); tincture of aconite, not less than 0.045 Gm. nor more than 0.055 Gm. in 100 mils. (or Cc.).

It must be borne in mind that aconitine is easily decomposed by application of a high heat, and hence evaporation of its solutions should be conducted at a moderate temperature.

Assay of Aconite.—Introduce 15 Gms. of aconite in No. 40 powder, into 250 mils. (or Cc.) flask and add 150 mils. (or Cc.) of ether. Stopper the flask, shake well and allow it to stand ten minutes, then add 5 mils. (or Cc.) of ammonia water and shake the flask vigorously every 10 minutes during 2 hours. Now add 15 mils. (or Cc.) of distilled water, again shake the flask well and when the drug has settled, decant exactly 100 mils. (or Cc.) of the clear liquid, representing 10 Gms. of the drug. Filter this liquid through a small pledget of absorbent cotton into a separator and rinse the graduated cylinder and cotton with a little ether. Completely extract the alkaloids from the solution by shaking out with successive portions of weak sulphuric acid, using for the first extraction 10 mils. (or Cc.) of half-normal acid and for the next three extractions a mixture of 5 mils. (or Cc.) each of half-normal acid and distilled water. Collect the acid washings in a separator, add ammonia water until the liquid is decidedly alkaline to litmus, and completely extract the alkaloids by shaking out with successive portions of ether (25, 15, 10 and 10 mils. (or Cc.)).

Having passed the successive ether washings through a small pledget of absorbent cotton, evaporate the whole carefully to dryness, soften the residue by addition of about 1 mil. (or Cc.) of neutral alcohol, or ether; add exactly 5 mils. (or Cc.) of tenth-normal sulphuric acid and warm the mixture gently to insure complete solution of the alkaloids.

Finally add sufficient distilled water to bring the volume of the liquid to about 25 mils. (or Cc.) and titrate the excess of acid with fiftieth-normal potassium hydroxide solution, using cochineal test-solution as indicator. Each mil. (or Cc.) of the tenth-normal acid consumed corresponds to 0.064539 Gm. of the ether-soluble alkaloids of aconite. Divide the number of mils. (or Cc.) of fiftieth-normal potassium hydroxide solution used by 5, subtract this quotient from 5 (the number of mils. (or Cc.) of tenth-normal acid added) and multiply the remainder by 0.64539 (0.064539 × 10), 10 Gms. of the drug having been represented by the 100 mils. (or Cc.) of liquid taken for the assay; the product will express the percentage of ether-soluble alkaloids in the drug examined.

Assay of Extract of Aconite.—Mix 3 Gms. of the powdered extract thoroughly with 10 Gms. of washed sand in a 250 mil. (or Cc.) flask, add 150 mils. (or Cc.) of ether and 2 mils. (or Cc.) of ammonia water, shake the mixture vigorously every few minutes during a half hour, and when the dregs have settled decant exactly 100 mils. (or Cc.) of the clear liquid, representing 2 Gms. of the extract. From this point proceed as directed in the assay of aconite given above, beginning with the words "Filter this liquid". The amount of alkaloids found by calculation when multiplied by 50 will express the percentage of ether-soluble alkaloids in the extract.

Assay of Fluidextract of Aconite.—Drop 15 mils. (or Cc.) of fluidextract of aconite from a pipette evenly over the surface of 15 Gms. of purified sawdust (see page 841) and evaporate to dryness at not exceeding 75° C. (167° F.). Transfer the mixture to a 250 mil. (or Cc.) flask, add 150 mils. (or Cc.) of ether and proceed as directed above for the assay of aconite, using the ammonia water there directed with a small quantity of distilled water to rinse the dish in which the sawdust mixture was evaporated. Having calculated the amount of ether-soluble alkaloids found in the 10 mils. (or Cc.) of fluidextract assayed, multiply this sum by 10 to ascertain the amount present in 100 mils. (or Cc.).

Assay of Tincture of Aconite.—Transfer 150 mils. (or Cc.) of tincture of aconite to an evaporating dish and evaporate to about 20 mils. (or Cc.) at not exceeding 75° C. (167° F.), and incorporate thoroughly with 10 Gms. of purified sawdust (see page 841), continuing the evaporation to dryness. From this point proceed as directed above for the assay of fluidextract of aconite. The amount of alkaloid found by calculation represents the amount of ether-soluble alkaloids in 100 mils. (or Cc.) of the tincture, since that volume (or ⅔ of the original volume taken) was represented in the final steps of the assay.

ASSAY OF BELLADONNA, HYOSCYAMUS AND STRAMONIUM AND THEIR PREPARATIONS.

These three mydriatic drugs containing practically the same alkaloids are tested by the same method of assay, and can therefore be considered under one general head. The Pharmacopœia makes the following requirements for the crude drugs and their preparations:

Belladonna leaves should contain not less than 0.30 per cent. of total alkaloids; belladonna plaster, not less than 0.35, nor more than 0.40 per cent.; belladonna root, not less than 0.45 per cent.; extract of belladonna leaves, not less than 1.18 per cent., nor more than 1.32 per cent.; fluidextract of belladonna root, not less than 0.405 Gm., nor more than 0.495 Gm. in 100 mils. (or Cc.); tincture of belladonna leaves, not less than 0.027 Gm., nor more than 0.033 Gm. in 100 mils. (or Cc.).

Hyoscyamus should contain not less than 0.065 per cent. of total alkaloids; extract of hyoscyamus, not less than 0.22 per cent., nor more than 0.28 per cent.; fluidextract of hyoscyamus, not less than 0.055 Gm. nor more than 0.075 Gm. in 100 mils. (or Cc.); tincture of hyoscyamus, not less than 0.0055 Gm., nor more than 0.0075 Gm., in 100 mils. (or Cc.). As hyoscyamus contains a very much smaller percentage of alkaloids than the other mydriatic drugs, a larger quantity of the drug and also of its preparations is required for assay.

Stramonium should contain not less than 0.25 per cent. of total alkaloids; extract of stramonium, not less than 0.9 per cent., nor more than 1.1 per cent.; tincture of stramonium, not less than 0.0225 Gm., nor more than 0.0275 Gm. in 100 mils. (or Cc.).

Assay of Belladonna (*Leaves or Root*), **or Stramonium.**—Introduce 15 Gms. of the drug, in No. 60 powder, into a 300 mil. (or Cc.) flask and add 150 mils. (or Cc.) of a mixture of chloroform, 1 volume, and ether, 2 volumes. Stopper the flask, shake it well and allow it to stand 10 minutes, then add 5 mils. (or Cc.) of ammonia water and shake vigorously every 10 minutes during 2 hours. Now add 25 mils. (or Cc.) of distilled water in the case of belladonna leaves and stramonium, or 15 mils. (or Cc.) in the case of belladonna root, shake the flask well, and when the drug has settled, decant exactly 100 mils. (or Cc.) of the clear solution, representing 10 Gms. of the drug. Filter the solution through a small pledget of absorbent cotton into a separator, and rinse the graduated cylinder and cotton with a little ether. Extract the alkaloids completely by shaking the solution out with weak sulphuric acid, using for the first extraction 10 mils. (or Cc.) of half-normal acid and for each of the next three extractions a mixture of 5 mils. (or Cc.) each of half-normal acid and distilled water. (The extraction should be continued until 0.5 mil. (or Cc.) of the acid washings shows only a very faint cloudiness on addition of a drop of Mayer's Solution.)

Collect the acid washings in a separator, add ammonia water until the liquid is distinctly alkaline to litmus and extract the alkaloids completely by shaking out repeatedly with chloroform, using 25, 15, 10, and 10 mils. (or Cc.). Having passed the successive chloroform washings through a small pledget of absorbent cotton, evaporate the whole to dryness, soften the residue by addition of about 1 mil. (or Cc.) of neutral alcohol or ether, add exactly 5 mils. (or Cc.) of tenth-normal sulphuric acid and warm the mixture gently to insure complete solution of the alkaloids. Finally add sufficient distilled water to bring the volume of the liquid up to about 25 mils. (or Cc.) and titrate the excess of acid with fiftieth-normal potassium hydroxide solution, using cochineal test-solution as indicator. (In the case of belladonna leaves and stramonium, the alkaloidal residue, before titration, should be treated twice with 5 mils. (or Cc.) of ether, evaporating to dryness each time.) As each mil. (or Cc.) of tenth-normal acid consumed corresponds to 0.02892 Gm. of mydriatic alkaloids, the percentage of the latter present in the drug may be determined by dividing the number of fiftieth-normal potassium hydroxide solution used by 5, subtracting this quotient from 5, the number of mils. (or Cc.) of tenth-normal acid added, and multiplying the remainder by 0.2892 (0.02892 × 10), 10 Gms. of the drug having been represented in the 100 mils. (or Cc.) of liquid taken for the assay.

Assay of Hyoscyamus.—The same method is employed for the assay of hyoscyamus as for the three preceding drugs, except that on account of the small yield of alkaloids, 30 Gms. of the drug, in No. 60 powder, is introduced into a 500 mil. (or Cc.) flask and 300 mils. (or Cc.) of a mixture of chloroform, 1 volume, and ether 2 volumes are added. After the 2 hours maceration directed in the case of belladonna and stramonium, 40 mils. (or Cc.) of distilled water are added, and when the drug has settled 200 mils. (or Cc.) of the clear liquid are decanted, representing 20 Gms. of hyoscyamus. From this point the process is the same as directed for belladonna and stramonium. In the final calculation for percentage of alkaloids, it must not be overlooked that 20 Gms. of drug are used in this case and hence the factor 0.02892 must be multiplied by 5 instead of 10.

Assay of Belladonna Plaster.—This process is intended not only for the assay of belladonna plaster mass, but also for the assay of spread belladonna plasters. In the former case introduce 10 Gms. of the plaster mass into a 100 mil. (or Cc.) flask, and in the case of spread plasters, cut the portion to be assayed into strips, weigh it accurately and introduce it into the flask. After adding 50 mils. (or Cc.) of chloroform, shake the mixture well until the plaster is dissolved, pour the chloroform solution into a 250 mil. (or Cc.) beaker and wash the cloth upon which the plaster was spread with 2 portions of 25 mils. (or Cc.) each of chloroform and add the washings to the chloroform

solution in the beaker. Then wash the cloth with 80 mils. (or Cc.) of alcohol containing 1 mil. (or Cc.) of ammonia water and pour the washings into the chloroform solution in the beaker. Stir the mixture gently and allow it to stand until the rubber has separated into a compact mass. Having dried the cloth upon which the belladonna plaster was spread, weigh it and subtract its weight from the original weight of the strips put into the flask.

The chloroform-alcohol solution is now poured into a 350 mil. (or Cc.) separator and the beaker and rubber rinsed with 10 mils. (or Cc.) of alcohol, the rinsings being added to the contents of the separator. Add 100 mils. (or Cc.) of distilled water to the separator, rotate until thoroughly mixed and allow it to stand until the liquids separate. Draw off the chloroform into a second separator containing 50 mils. (or Cc.) of distilled water, shake thoroughly and after separation draw off the chloroform into a beaker and pour the aqueous solution into the first separator. Return the chloroform solution to the second separator and shake out the contents of the first separator with 2 portions of 10 and 5 mils. (or Cc.) respectively of chloroform, adding them to the chloroform in the second separator.

Completely extract the alkaloids from the chloroform solution by shaking it out repeatedly with weak sulphuric acid, using for the first extraction 10 mils. (or Cc.) of half-normal acid and for the next three extractions a mixture of 5 mils. (or Cc.) of half-normal acid and 5 mils. (or Cc.) of distilled water. Collect the acid washings in a separator and add ammonia water until the solution is decidedly alkaline to litmus, and completely extract the alkaloids by shaking repeatedly with chloroform, using 25, 15, 10 and 10 mils. (or Cc.) of the latter. Filter the successive chloroform solutions through a small pledget of absorbent cotton, evaporate to dryness and dissolve the alkaloids from the residue in exactly 5 mils. (or Cc.) of tenth-normal sulphuric acid and titrate the excess of acid with fiftieth-normal potassium hydroxide solution, using cochineal test-solution as indicator. As each mil. (or Cc.) of tenth-normal acid consumed corresponds to 0.02892 Gm. of mydriatic alkaloids, the percentage of the latter present in the plaster may be determined by dividing the number of fiftieth-normal potassium hydroxide solution used by 5, subtracting this quotient from 5, the number of mils. (or Cc.) of tenth-normal acid added, and multiplying the remainder by 2.892 (0.02892×100) and then dividing this product by the weight of plaster mass originally taken, or the weight of mass found to have been on the strips of spread plaster used for the assay.

The object of adding alcohol to the chloroformic solution is to precipitate the rubber and at the same time keep the liberated alkaloids in solution. In order to insure solution of all the alkaloid, it will be found desirable to redissolve the precipitate of rubber in a fresh portion of chloroform and again treat with alcohol as before, adding the second alcoholic solution to the first.

Assay of Extract of Belladonna Leaves, or of Stramonium.—The Pharmacopœia recognizing both pilular and powdered extracts of belladonna leaves and stramonium gives different methods for their assay, thus:

For the Pilular Extracts.—Dissolve 2 Gms. of the extract in 10 mils. (or Cc.) of diluted alcohol, transfer the solution to a separator and wash the dish with a mixture of 2 mils. (or Cc.) of ammonia water and 10 mils. (or Cc.) of distilled water in divided portions, adding the washings to the contents of the separator. From this point proceed as directed in the assay of fluidextract of belladonna root, beginning with the words "Completely extract the alkaloids;" when the dry alkaloidal residue has been obtained, however, treat the same twice with 5 mils. (or Cc.) of ether, evaporating to dryness each time, before proceeding further. The weight of alkaloids found by calculation after titration, when multiplied by 50 will express the percentage of alkaloids present in the sample of extract.

For the Powdered Extracts.—Mix 3 Gms. of the extract thoroughly with 10 Gms. of washed sand, introduce into a 250 mil. (or Cc.) flask, add 150 mils. (or Cc.) of a mixture of chloroform, 1 volume, and ether, 2 volumes, followed by 5 mils. (or Cc.) of ammonia water. Shake vigorously every 10 minutes during a half hour and when the dregs have settled, decant 100 mils. (or Cc.) representing 2 Gms. of the extract. From this point proceed as directed in the assay of belladonna leaves and root, on page 846, beginning with the words "Filter the solution," but before titration of the alkaloidal residue treat the same twice with 5 mils. (or Cc.) of ether, evaporating to dryness each time. The calculation is the same as for pilular extracts.

Assay of Extract of Hyoscyamus.—The method employed for the assay of this extract is identical with that given above for the assay of the pilular extracts of belladonna leaves and stramonium, except that 5 Gms. of extract of hyoscyamus are taken for the assay instead of 2 Gms., and the weight of alkaloids finally found by calculation must be multiplied by 20 instead of 50 to ascertain the percentage of total alkaloids in the extract.

Assay of Fluidextract of Belladonna Root.—Measure 10 mils. (or Cc.) of the fluidextract into a separator and add 10 mils. (or Cc.) of distilled water and 2 mils. (or Cc.) of ammonia water. Completely extract the alkaloids by shaking out with successive portions of chloroform (using 25, 15, 10 and 10 mils. (or Cc.) or more if necessary) and testing the last extraction with Mayer's Solution. Having passed the chloroform solutions successively through a small pledget of absorbent cotton into another separator, shake out with successive portions of weak sulphuric acid, using for the first extraction 10 mils. (or Cc.) of half-normal acid and for each of the next three extractions a mixture of 5 mils. (or Cc.) of half-normal acid and 5 mils. (or Cc.) of distilled

water. (The extraction should be continued until 0.5 mil. (or Cc.) of the acid washings shows barely a faint cloudiness on addition of a drop of mercuric potassium iodide test-solution.) Collect the acid washings in a separator, add ammonia water until the liquid is decidedly alkaline to litmus, and extract the alkaloids completely by shaking out with successive portions of chloroform. Evaporate the combined chloroform washings to dryness, dissolve the alkaloids from the residue in exactly 5 mils. (or Cc.) of tenth-normal sulphuric acid and titrate the excess of acid with fiftieth-normal potassium hydroxide solution, using cochineal test-solution as indicator. Each mil. (or Cc.) of the tenth-normal acid consumed corresponds to 0.02892 Gm. of belladonna alkaloids.

Before adding the tenth-normal acid it is advisable to soften the alkaloidal residue with 1 mil. (or Cc.) of neutral alcohol or ether and then after addition of the acid to warm the mixture gently to insure complete solution of the alkaloids; finally add sufficient distilled water to bring the volume of the liquid up to about 25 mils. (or Cc.) and then begin titration.

To ascertain the amount of alkaloids in 100 mils. (or Cc.) of the fluidextract, multiply the amount found by assay in 10 mils. (or Cc.) by 10.

Assay of Fluidextract of Hyoscyamus.—The method given above for the assay of the fluidextract of belladonna root, may also be used for this fluidextract, except that 25 mils. (or Cc.) of fluidextract of hyoscyamus are directed to be used, and that before titration of the alkaloidal residue, the same is treated twice with 5 mils. (or Cc.) of ether, evaporating to dryness each time. To ascertain the amount of total alkaloids in 100 mils. (or Cc.) of the fluidextract, multiply the amount found by calculation in the 25 mils. (or Cc.) used for the assay, by 4.

Assay of Tincture of Belladonna Leaves, or of Stramonium.—Evaporate 100 mils. (or Cc.) of the respective tincture on a water bath until the liquid measures about 10 mils. (or Cc.) Transfer the liquid to a separator and rinse the dish with a mixture of 5 mils. (or Cc.) of ammonia water and 5 mils. (or Cc.) of distilled water in divided portions, adding the rinsings to the contents of the separator. From this point proceed as directed for the assay of fluidextract of belladonna root on page 849, beginning with the words "Completely extract the alkaloids". Before titrating the alkaloidal residue treat the same twice with 5 mils. (or Cc.) of ether, evaporating to dryness each time. The amount of alkaloids found by calculation represents the amount present in 100 mils. (or Cc.)

Assay of Tincture of Hyoscyamus.—The Pharmacopœia directs this tincture to be assayed exactly in the same manner as the preceding

two tinctures, but on account of the very small percentage of alkaloid in the drug, it will be found preferable to use 250 mils. (or Cc.) of the tincture, which should be evaporated to about 10 mils. (or Cc.), and the process then continued exactly as given above for the assay of tincture of belladonna leaves. The resulting product must be divided by 2.5 to ascertain the weight of alkaloids contained in 100 mils. (or Cc.) of the tincture.

ASSAY OF CINCHONA AND ITS PREPARATIONS.

The alkaloidal value of cinchona is preferably determined gravimetrically on account of the number of alkaloids present, which would cause unsatisfactory and unreliable results by the volumetric method. The Pharmacopœia requires that cinchona, as well as red cinchona, shall contain not less than 5 per cent. of total alkaloids, dried to constant weight at 100° C. (212° F.). It also requires that fluidextract of cinchona shall contain in 100 mils. (or Cc.) not less than 4 Gms. nor more than 5 Gms. of total cinchona alkaloids; tincture of cinchona, not less than 0.8 Gm. nor more than 1 Gm. in 100 mils. (or Cc.) and compound tincture of cinchona, not less than 0.4 Gm. nor more than 0.5 Gm. in 100 mils. (or Cc.).

Assay of Cinchona.—Introduce 5 Gms. of cinchona, in No. 40 powder, into a 500 mil. (or Cc.) flask and add 200 mils. (or Cc.) of a mixture of chloroform 1 volume, and ether, 2 volumes. Having stoppered the flask, shake it well and let it stand 10 minutes. Then add 5 mils. (or Cc.) of ammonia water, shake the flask frequently for 1 hour and set it aside for 8 or 10 hours. Now add 10 mils. (or Cc.) of distilled water, shake the mixture vigorously and when the drug has settled, decant 160 mils. (or Cc.) of the clear solution, representing 4 Gms. of cinchona. Filter the liquid through a small pledget of absorbent cotton into a separator, rinsing the graduated cylinder and cotton with ether. Completely extract the alkaloids from the chloroform-ether solution by shaking out repeatedly with weak sulphuric acid (see Assay of Belladonna Root). Collect the acid washings in a separator, add ammonia water until the solution is distinctly alkaline to litmus, and completely extract the alkaloids by shaking out repeatedly with chloroform (using 25, 15, 10 and 10 mils. (or Cc.), or more if necessary). Filter the successive portions of chloroform solution through a small pledget of absorbent cotton into a tared flask, and wash the funnel and cotton with chloroform. Evaporate the chloroform solution on a waterbath, add 5 mils. (or Cc.) of alcohol to the residue, and again evaporate. Repeat the evaporation with alcohol and dry the residue at 100° C. (212° F.) to constant weight. If the weight thus obtained is multiplied by 25, the product will express the percentage of total alkaloids present in the sample of cinchona.

Assay of Fluidextract of Cinchona.—Carefully measure 5 mils. (or Cc.) of fluidextract of cinchona in a pipette and allow the same to drop evenly over the surface of 10 Gms. of purified sawdust (see footnote on page 841), and evaporate to dryness at a temperature not exceeding 80° C. (176° F.). Transfer the dry powder to a 500 mil. (or Cc.) flask and add 200 mils. (or Cc.) of a mixture of chloroform, 1 volume, and ether, 2 volumes. Rinse the dish with 10 mils. (or Cc.) of ammonia water and add the rinsings to the contents of the flask. From this point proceed exactly as directed for the assay of cinchona, beginning with the words "shake the flask frequently". The weight of alkaloids obtained, when multiplied by 25 will represent the amount of total alkaloids in 100 mils. (or Cc.) of the fluidextract.

Assay of Tincture of Cinchona.—Having evaporated 25 mils. (or Cc.) of tincture of cinchona on a waterbath to about 15 mils. (or Cc.), add 10 Gms. of purified sawdust (see footnote on page 841), incorporate thoroughly and evaporate to dryness at a temperature not exceeding 80° C. (176° F.). Transfer the dry mixture to a 500 mil. (or Cc.) flask and add 200 mils. (or Cc.) of a mixture of chloroform, 1 volume, and ether, 2 volumes. Rinse the dish with 10 mils (or Cc.) of ammonia water and add the rinsings to the contents of the flask. From this point proceed exactly as directed for the assay of cinchona, beginning with the words "shake the flask frequently". The weight of alkaloids obtained, when multiplied by 5 will represent the amount of total alkaloids in 100 mils. (or Cc.) of the tincture.

Assay of Compound Tincture of Cinchona.—This tincture can be assayed in the same manner as directed above for the simple tincture of cinchona, except that 50 mils. (or Cc.) of the compound tincture should be used instead of 25, and that the final weight of dried alkaloids must be multiplied by 2.5 instead of 5, to ascertain the amount present in 100 mils. (or Cc.) of the compound tincture.

ASSAY OF COLCHICUM CORM AND SEED AND THEIR PREPARATIONS.

The determination of alkaloidal content in colchicum and its preparations is best made gravimetrically. The Pharmacopœia requires that colchicum corm shall contain not less than 0.35 per cent. of colchicine, and colchicum seed not less than 0.45 per cent.; also that extract of colchicum corm shall contain not less than 1.25 per cent., nor more than 1.55 per cent. of colchicine; fluidextract of colchicum seed not less than 0.36 Gm., nor more than 0.44 Gm. of colchicine in 100 mils. (or Cc.), and tincture of colchicum seed not less than 0.036 Gm., nor more than 0.044 Gm. of colchicine in 100 mils. (or Cc.).

Assay of Colchicum Corm and Seed.—Having introduced 15 Gms. of colchicum corm or seed, in No. 60 powder, in a 500 mil. (or Cc.) flask, add 10 mils. (or Cc.) of lead subacetate solution and 290 mils. (or Cc.) of distilled water. Weigh the flask and contents, and digest the mixture at from 60° to 70° C. (140° to 188° F.) for 3 hours, with occasional agitation. Cool and add sufficient distilled water to restore the original weight. Filter off 200 mils. (or Cc.) and add 0.75 Gm. of sodium phosphate to the clear filtrate, shake the mixture frequently during a half hour and filter off 100 mils. (or Cc.) representing 5 Gms. of the drug. Shake out the alkaloid from the filtrate with successive portions of chloroform until completely extracted, as shown by testing with iodine test-solution, and evaporate the combined chloroform solutions in a tared flask; to the residue add about 1 mil. (or Cc.) of alcohol and again evaporate. Repeat this operation once more and dry the residue to constant weight at 100° C. (212° F.). To the weighed residue in a flask add 5 mils. (or Cc.) of tenth-normal sulphuric acid and 5 mils. (or Cc.) of distilled water and heat the mixture for 10 minutes at 70° C. (188° F.). Filter through a small pledget of absorbent cotton and wash the cotton with distilled water. Reject the filtrate and washings, removing as much of the water from the cotton as possible, and dissolve any insoluble residue that may remain on the cotton by washing it first with a little alcohol and then with ether. Collect the alcohol-ether washings in the flask, evaporate, dry to constant weight at 100° C. (212° F.) and weigh. Deduct this weight from the weight of residue previously obtained; the difference will be the weight of colchicine found in 5 Gms. of the drug. This weight, when multiplied by 20 represents the percentage of colchicine in the sample assayed.

Assay of Extract of Colchicum Corm.—This powdered extract is directed to be assayed exactly in the same manner as the crude drug, except that 6 Gms. of the extract shall be used instead of 15 Gms. of the corm or seed. As but 2 Gms. of the extract are represented in the final steps of the assay, the weight of colchicine obtained must be multiplied by 50 to ascertain the percentage present in the extract.

Assay of Fluidextract of Colchicum Seed.—Having introduced 15 mils. (or Cc.) of fluidextract of colchicum seed into a 500 mil. (or Cc.) flask, add 10 mils. (or Cc.) of lead subacetate solution mixed with 35 mils. (or Cc.) of distilled water. Shake thoroughly and then add 240 mils. (or Cc.) of distilled water and again shake the mixture. From this point proceed as directed for the assay of colchicum corm and seed (see above), beginning with the words "Filter off 200 mils. (or Cc.)". As but 5 mils. (or Cc.) of the fluidextract are represented in the final steps of the assay, the weight of colchicine obtained must be multiplied by 20 to ascertain the amount present in 100 mils. (or Cc.).

Assay of Tincture of Colchicum Seed.—Evaporate 150 mils. (or Cc.) of tincture of colchicum seed on a waterbath to about 20 mils. (or Cc.), transfer it to a 50 mil. (or Cc.) graduated flask and rinse the dish with about 10 mils. (or Cc.) of distilled water, in divided portions, adding the rinsings to the contents of the flask. Add 10 mils. (or Cc.) of lead subacetate solution, shake thoroughly and then add sufficient distilled water to bring the volume exactly up to 50 mils. (or Cc.). Pour the mixture into a 500 mil. (or Cc.) flask, add 250 mils. (or Cc.) of recently boiled distilled water, using a part of the water to rinse the 50 mil. (or Cc.) flask and proceed from this point exactly as directed for the assay of colchicum corm and seed, beginning with the words "Filter off 200 mils. (or Cc.)". As only 50 mils. (or Cc.) of the original tincture are represented in the final steps of the assay, the weight of colchicine obtained must be multiplied by 2 to ascertain the amount present in 100 mils. (or Cc.).

ASSAY OF GUARANA AND ITS PREPARATIONS.

Since the active principles of guarana, chiefly caffeine, can be obtained in quite pure form, the Pharmacopœia directs that the assay of the drug and its preparations shall be made gravimetrically, and requires that guarana shall contain not less than 4 per cent. of caffeine and fluidextract of guarana not less than 3.6 Gms. nor more than 4.4 Gms. of the same in 100 mils. (or Cc.).

Assay of Guarana.—Put 6 Gms. of guarana, in No. 60 powder, into a flask and pour upon it 120 mils. (or Cc.) of chloroform and 6 mils. (or Cc.) of ammonia water. Shake frequently for half an hour, and let stand for four hours. Again shake the flask vigorously and when the drug has settled, filter the liquid rapidly through a small pledget of absorbent cotton and collect 100 mils. (or Cc.) of filtrate representing 5 Gms. of guarana. Evaporate the clear filtrate to dryness and dissolve the residue in weak sulphuric acid with the aid of a gentle heat. When the liquid has cooled, filter into a separator and wash the container and filter with several portions of distilled water. Now add ammonia water until the liquid is distinctly alkaline to litmus and shake out the caffeine with chloroform until completely extracted, as shown by testing with iodine test-solution. Evaporate the united chloroform solutions and dry the residue to constant weight at 80° C. (176° F.). The weight obtained when multiplied by 20 will represent the percentage of caffeine in the drug.

The weak acid prescribed in this assay may be made by mixing 2 mils. (or Cc.) of normal sulphuric acid with 20 mils. (or Cc.) of distilled water. It will be found advantageous to shake out the caffeine with 4 successive portions (20, 10, 10 and 10 mils. (or Cc.) of chloroform.

Assay of Fluidextract of Guarana.—Transfer to a separator 5 mils. (or Cc.) of fluidextract of guarana, add 1 mil. (or Cc.) of ammonia water, and shake out the alkaloid with successive portions of chloroform until completely extracted, as shown by testing with iodine test-solution. Evaporate the combined chloroform solutions to dryness and dissolve the residue in 20 mils. (or Cc.) of distilled water with the aid of heat. Allow this to cool, filter it into a separator and wash the container and filter with several small portions of distilled water, adding the rinsings to the liquid in the separator. Then shake out the alkaloid with chloroform until completely extracted, as shown by testing with iodine test-solution, evaporate the combined chloroform solutions and dry the residue to constant weight at 80° C. (176° F.). The weight of caffeine obtained, when multiplied by 20 will represent the amount present in 100 mils. (or Cc.) of the fluidextract.

ASSAY OF HYDRASTIS AND ITS PREPARATIONS.

Although hydrastis contains three alkaloids, berberine, canadine, and hydrastine, the medicinal virtues of the drug seem to reside wholly in the latter, and hence the determination of its content is an excellent criterion for the valuation of the drug. The Pharmacopœia requires that hydrastis shall contain not less than 2.5 per cent. of the ether-soluble alkaloids of hydrastis; extract of hydrastis, not less than 9 nor more than 11 per cent.; fluidextract of hydrastis, not less than 1.8 Gms., nor more than 2.2. Gms. in 100 mils. (or Cc.); glycerite of hydrastis, not less than 1.12 Gms., nor more than 1.37 Gms. in 100 mils. (or Cc.); tincture of hydrastis, not less than 0.36 Gm., nor more than 0.44 Gm. in 100 mils. (or Cc.). All determinations are made gravimetrically.

Hydrastine exists in the drug partly in the free and partly in the combined state, and advantage is taken in the official method of assay of the fact that berberine is practically insoluble in ether. While hydrastine is colorless, it will be found almost impossible to obtain the alkaloid entirely free from a slight yellow color, which is due to traces of berberine.

Assay of Hydrastis.—Ten Gms. of hydrastis, in No. 60 powder, are introduced into a 250 mil. (or Cc.) flask and 100 mils. (or Cc.) of ether then added; the flask is stoppered and the mixture well shaken and allowed to stand for 10 minutes, after which 5 mils. (or Cc.) of ammonia water are added and the flask vigorously shaken every 10 minutes during 2 hours. From this point proceed as directed for the assay of belladonna root on page 846, beginning with the words "Now add 25 mils. (or Cc.)". Modify the process for belladonna root by using only 50 mils. (or Cc.) of the ether solution, representing 5 Gms. of hydrastis to complete the assay and use ether throughout the process instead of chloroform. The final combined ether solutions are evapo-

rated to dryness and then to constant weight at 100° C. (212° F.). The weight of alkaloids obtained when multiplied by 20 will represent the percentage of ether-soluble alkaloids in the drug.

Assay of Extract of Hydrastis.—Mix 3 Gms. of the powdered extract of hydrastis thoroughly with 10 Gms. of washed sand and introduce into a 250 mil. (or Cc.) flask. Having added 150 mils. (or Cc.) of ether and 5 mils. (or Cc.) of ammonia water, shake the mixture vigorously every 10 minutes during a half hour, and when the drugs have settled decant 100 mils. (or Cc.) of the clear liquid, representing 2 Gms. of the extract. From this point proceed as directed for the assay of belladonna root on page 846, beginning with the words "Filter the solution". Modify the process for belladonna root by using ether throughout the process and dry the final residue to constant weight at 100° C. (212° F.). The weight of alkaloids obtained when multiplied by 50 will represent the percentage of ether-soluble alkaloids of hydrastis in the extract.

Assay of Fluidextract of Hydrastis.—Proceed exactly as directed for the assay of fluidextract of belladonna root on page 849, modifying the process there given by using only 5 mils. (or Cc.) of fluidextract instead of 10, and using only ether throughout as the immiscible solvent. Dry the residue to constant weight instead of titrating it. The weight of alkaloids obtained, when multiplied by 20 will represent the amount of ether-soluble alkaloids in 100 mils. (or Cc.) of the fluidextract.

Assay of Glycerite of Hydrastis.—Proceed as directed for the assay of fluidextract of belladonna root on page 849, modifying the process there given by using 5 mils. (or Cc.) of glycerite of hydrastis instead of 10 mils. (or Cc.) of fluidextract of belladonna root and use only ether as the immiscible solvent throughout the assay. Wash the final ether extractions with 10 mils. (or Cc.) of distilled water, draw off the water and discard it. Then filter the ether solution through a small pledget of absorbent cotton, wash the cotton with ether, evaporate the filtrate and washings, and dry the residue at 100° C. (212° F.) to constant weight instead of titrating it. The weight of alkaloids obtained, when multiplied by 20 will represent the amount of ether-soluble alkaloids in 100 mils. (or Cc.) of the glycerite.

Assay of Tincture of Hydrastis.—Evaporate 50 mils. (or Cc.) of tincture of hydrastis on a waterbath to about 10 mils. (or Cc.) and transfer the liquid to a separator. From this point proceed as directed for the assay of fluidextract of belladonna root on page 849, beginning with the words "and add 10 mils. (or Cc.)," except that the 2 mils. (or Cc.) of ammonia water are diluted with 5 mils. (or Cc.) of distilled water and then used to rinse out the evaporating dish, adding the

rinsings to the contents of the separator. Ether only is used in the process and the alkaloidal residue is to be dried at 100° C. (212° F.) and then weighed. The weight of alkaloids obtained when multiplied by 2 represents the amount of ether-soluble alkaloids in 100 mils. (or Cc.) of the tincture.

ASSAY OF IPECAC AND ITS PREPARATIONS.

The chief alkaloids found in ipecac are cephaeline and emetine or methylcephaeline, together with a very small amount of psychotrine. Although they are not always present in the same proportions, the Pharmacopœia by giving the equivalent of combined ipecac alkaloids for tenth-normal sulphuric acid as 0.024 Gm. for each mil. (or Cc.) recognizes only the two first-named and as present in equal proportions, for the equivalent of cephaeline for the acid is 0.023316 Gm. and for emetine 0.024718 Gm., the mean of which is 0.0240 Gm. The alkaloid psychotrine, being insoluble in ether will be left in the dregs. It is possible to separate the cephaeline from the emetine by the solubility of the former in sodium hydroxide solution and then to determine the exact quantity of each present in any sample of ipecac, but for purposes of valuation of the drug this more tedious method is quite unnecessary. The official requirements are that ipecac shall contain not less than 1.75 per cent. of the ether-soluble alkaloids, and the fluidextract of ipecac, not less than 1.8 Gms., nor more than 2.2 Gms. of the same in 100 mils. (or Cc.).

Assay of Ipecac.—Introduce 10 Gms. of ipecac, in No. 80 powder, into a 250 mil. (or Cc.) flask, add 100 mils. (or Cc.) of ether and proceed as directed for the assay of belladonna root, on page 846, beginning with the words "Stopper the flask," modifying the process there given by using 50 mils. (or Cc.) of the ether solution, representing 5 Gms. of ipecac, to complete the assay. Ether is used throughout the process and the alkaloidal residue is dissolved in 10 mils. (or Cc.) of tenth-normal sulphuric acid. As each mil. (or Cc.) of the tenth-normal acid corresponds to 0.024 Gm. of ether-soluble ipecac alkaloids, the number of mils. (or Cc.) consumed, when multiplied by 2.4 (0.024×100) and divided by 5 will express the percentage of alkaloids present in the drug.

Assay of Fluidextract of Ipecac.—Measure 10 mils. (or Cc.) of fluidextract of ipecac in a pipette and allow it to drop evenly over the surface of 10 Gms. of purified sawdust (see footnote on page 841), and dry the mixture at a temperature not exceeding 80° C. (176° F.). Having transferred the impregnated sawdust to a 250 mil. (or Cc.) flask, add 100 mils. (or Cc.) of ether and rinse the dish in which the mixture was dried with a mixture of 6 mils. (or Cc.) of ammonia water and an equal volume of water, in divided portions, adding the rinsings

to the contents of the flask. Stopper the flask and shake it vigorously every few minutes during 2 hours. Now add 15 mils. (or Cc.) of distilled water, again shake the flask well, and when the dregs have settled, decant 50 mils. (or Cc.) of the ether solution, representing 5 mils. (or Cc.) of the fluidextract. Filter the ethereal solution through a small pledget of absorbent cotton into a separator, washing the graduated cylinder and cotton with a little ether, and shake out the alkaloids with weak sulphuric acid, as directed in the assay of fluidextract of belladonna root on page 849. Collect the acid washings in a separator, add ammonia water until the liquid is decidedly alkaline to litmus and completely extract the alkaloids by shaking out with successive portions of ether. Evaporate the combined ether washings to dryness, dissolve the alkaloidal residue in exactly 10 mils. (or Cc.) of tenth-normal sulphuric acid and titrate the excess of acid with fiftieth-normal potassium hydroxide solution, using cochineal test-solution as indicator. Divide the number of mils. (or Cc.) of the fiftieth-normal alkali solution used by 5 and subtract the quotient from 10 to ascertain the number of mils. (or Cc.) of tenth-normal acid consumed by the alkaloids. Each mil. (or Cc.) of tenth-normal acid consumed corresponds to 0.024 Gm. of the ether-soluble alkaloids of ipecac. The amount of alkaloids found in the 5 mils. (or Cc.) of fluidextract, when multiplied by 20 will express the amount present in 100 mils. (or Cc.).

ASSAY OF NUX VOMICA AND ITS PREPARATIONS.

Nux vomica contains brucine and strychnine in approximately equal proportions and the Pharmacopœia directs that the drug shall contain not less than 2.5 per cent. of total alkaloids; extract of nux vomica, not less than 15.2 nor more than 16.8 per cent.; fluidextract of nux vomica not less than 2.37 Gms. nor more than 2.63 Gms. in 100 mils. (or Cc.); tincture of nux vomica, not less than 0.237 Gm. nor more than 0.263 Gm. in 100 mils. (or Cc.).

Assay of Nux Vomica.—Having introduced 15 Gms. of nux vomica, in No. 40 powder, into a 250 mil. (or Cc.) flask, add 150 mils. (or Cc.) of a mixture of chloroform 1 volume, and ether, 2 volumes. Stopper the flask, shake it well and allow it to stand 10 minutes, then add 10 mils. (or Cc.) of ammonia water and, after shaking the flask vigorously every 10 minutes during 2 hours, allow it to stand for 10 hours. Now add 25 mils. (or Cc.) of distilled water, again shake the flask well, and when the drug has settled, decant 100 mils. (or Cc.) of the solution, representing 10 Gms. of nux vomica, and proceed from this point as directed for the assay of belladonna root on page 846, beginning with the words "Filter the solution". For the titration, dissolve the alkaloids from the residue with 10 mils. (or Cc.) of tenth-normal sulphuric acid. Each mil. (or Cc.) of tenth-normal acid consumed corresponds to 0.0364

Gm. of the total alkaloids, and the amount found by calculation to be in the 10 Gms. of drug assayed, when multiplied by 10 will express the percentage present in the drug.

Assay of Extract of Nux Vomica.—Thoroughly mix 3 Gms. of powdered extract of nux vomica with 10 Gms. of washed sand and introduce the mixture into a 250 mil. (or Cc.) flask. Then add 150 mils. (or Cc.) of a mixture of chloroform, 1 volume, and ether, 2 volumes, and 5 mils. (or Cc.) of ammonia water. Shake the mixture vigorously every 10 minutes during a half hour, and when the dregs have settled decant 100 mils. (or Cc.) of the clear liquid, representing 2 Gms. of the extract. From this point proceed as directed for the assay of belladonna root on page 846, beginning with the words "Filter the solution" and modifying the process by dissolving the alkaloidal residue in 10 mils. (or Cc.) of tenth-normal sulphuric acid instead of 5. Each mil. (or Cc.) of the tenth-normal acid consumed corresponds to 0.0364 Gm. of the total alkaloids of nux vomica. The amount of alkaloid found by calculation to have been in the 2 Gms. of extract, when multiplied by 50 will express the percentage of total alkaloids present in the extract.

Assay of Fluidextract of Nux Vomica.—Transfer 10 mils. (or Cc.) of fluidextract of nux vomica to a separator and add 10 mils. (or Cc.) of distilled water and 2 mils. (or Cc.) of ammonia water. Shake well and proceed as directed for the assay of fluidextract of belladonna root on page 849, beginning with the words "Completely extract the alkaloids". Modify the process by dissolving the alkaloidal residue in 10 mils. (or Cc.) of tenth-normal sulphuric acid instead of 5. As each mil. (or Cc.) of the tenth-normal acid consumed corresponds to 0.03642 Gm. of total alkaloids of nux vomica, the amount found by calculation to have been in the 10 mils. (or Cc.) of fluidextract assayed, when multiplied by 10 will express the amount in 100 mils. (or Cc.).

Assay of Tincture of Nux Vomica.—Having evaporated 100 mils. (or Cc.) of tincture of nux vomica on a waterbath to about 10 mils. (or Cc.) transfer the same to a separator and rinse the dish with a mixture of 5 mils. (or Cc.) of ammonia water and an equal volume of distilled water, in divided portions, adding the rinsings to the contents of the separator. From this point proceed as directed for the assay of fluidextract of belladonna root on page 849, beginning with the words "Completely extract the alkaloids". Modify the process by dissolving the alkaloidal residue in 10 mils. (or Cc.) of tenth-normal sulphuric acid instead of 5. Each mil. (or Cc.) of the tenth-normal acid consumed corresponds to 0.03642 Gm. of total alkaloids of nux vomica and the amount ascertained by calculation as present in the residue represents the amount in 100 mils. (or Cc.) of the tincture.

ASSAY OF OPIUM AND ITS PREPARATIONS.

The valuation of opium is always made on the basis of its morphine content, and the Pharmacopœia demands that the morphine extracted be weighed in the form of anhydrous crystals. It requires that opium in the moist state shall yield not less than 9.5 per cent. of anhydrous morphine, and when dried and in fine or granular powder, not less than 10, and not more than 10.5 per cent. Deodorized opium should yield the same percentage of anhydrous morphine as powdered opium. Extract of opium is required to yield not less than 19.5 per cent. nor more than 20.5 per cent. of anhydrous morphine, and tincture of opium, as well as tincture of deodorized opium, must contain not less than 0.95 Gm. nor more than 1.05 Gms. of anhydrous morphine in 100 mils. (or Cc.).

Assay of Opium.—Introduce 8 Gms. of opium, which, if fresh, should be in very small pieces, and if dry, in very fine powder, into an Erlenmeyer flask having a capacity of about 250 mils. (or Cc.), add 80 mils. (or Cc.) of distilled water, cork it well, and agitate every ten minutes, or in a mechanical shaker, during three hours. Then pour the whole as evenly as possible upon a wetted filter having a diameter of 12 cm., and, when the liquid has drained off, wash the residue with distilled water, carefully dropped upon the edges of the filter and its contents, until 120 mils. (or Cc.) of filtrate are obtained. Then carefully transfer the moist opium to a mortar by means of a spatula and rub to a smooth paste; rinse into the original flask with 50 mils. (or Cc.) of distilled water, agitate it thoroughly and return the whole to the filter. When the liquid has drained off, wash the residue with 75 mils. (or Cc.) of distilled water. Evaporate the filtrate and washings on a waterbath to about 40 Gms. Transfer the extract to a 50 mil. (or Cc.) graduated flask and wash the evaporating dish with sufficient water to make the entire volume exactly 50 mils. (or Cc.) when cooled to room temperature. Place in a small mortar 4 Gms. of freshly slaked lime, add about 10 mils. (or Cc.) of the opium extract and rub to a smooth paste, then add the remainder of the solution and rinse the flask with exactly 10 mils. (or Cc.) of distilled water, adding the rinsings to the contents of the mortar, and stir frequently for 15 minutes, avoiding unnecessary loss by evaporation. Filter through a dry filter, about 10 cm. in diameter, and transfer exactly 30 mils. (or Cc.) of the filtrate, representing 4 Gms. of opium, to an Erlenmeyer flask of suitable size. Add to the liquid 2 mils. (or Cc.) of alcohol and 15 mils. (or Cc.) of ether, and after shaking the mixture, add 1 Gm. of ammonium chloride and shake the flask frequently during a half-hour. Set the flask aside in a cool place for 12 hours or over night.

Remove the stopper and brush any adhering crystals back into the flask. Decant the ethereal layer into a small funnel, the neck of which has been previously closed with a pledget of absorbent cotton. Rinse the flask and contents with 15 mils. (or Cc.) of ether and when

the ether has passed through, wash the funnel and cotton with a small quantity of ether, then pour the aqueous liquid into the funnel without trying to remove the crystals. Wash the crystals in the flask and the contents of the funnel with distilled water previously saturated with morphine, until the washings are colorless. Then add a few drops of distilled water to replace the morphinated water. Incline the edge of the funnel over the mouth of the flask and by means of a glass rod carefully transfer the cotton with adhering crystals to the flask. Insert the funnel into the neck of the flask and wash the funnel with 20 mils. (or Cc.) of tenth-normal sulphuric acid, followed by 10 mils. (or Cc.) of distilled water applied drop by drop around the edge of the funnel. Remove the funnel, replace the cork, warm gently, and agitate until the crystals are dissolved. Rinse the cork with distilled water and titrate the excess of acid with fiftieth-normal potassium hydroxide solution, using cochineal test-solution as indicator. Each mil. (or Cc.) of the tenth-normal acid consumed corresponds to 0.028516 Gm. of anhydrous morphine.

Divide the number of mils. (or Cc.) of fiftieth-normal alkali solution required by 5, subtract the quotient from 20 (the number of mils. (or Cc.) of tenth-normal acid added) and multiply the remainder by 2.8516 (0.028516 × 100); this sum divided by 4, the weight of opium in Gms. represented in the 30 mils. (or Cc.) of liquid used for the assay, will express the percentage of anhydrous morphine in the opium.

Morphine being present in opium as meconate and sulphate is readily extracted with water; but along with it other substances, such as codeine, narceine, coloring matter, inorganic salts, etc., are also brought into solution, which it is intended to remove entirely or retain in solution by the addition of alcohol and ether when the precipitation of morphine is finally effected. As pure morphine is not entirely insoluble in water, a dilute mother-liquor is undesirable; hence concentration of the infusion is resorted to in order to reduce the loss from this source; the addition of alcohol has been found advantageous in preventing the precipitation of coloring matter along with the morphine, and is by no means hurtful in the proportion directed; the ether removes the codeine and other ether-soluble alkaloids present.

When freshly slaked lime is added to the concentrated infusion it decomposes the natural morphine salts, the liberated morphine being held in solution by the newly formed calcium hydroxide solution. The addition of ammonium chloride causes the formation of calcium chloride with liberation of ammonia, which latter then causes precipitation of the morphine alkaloid in a crystalline form, the separation being materially aided by active shaking of the flask as directed in the official assay process.

Assay of Extract of Opium.—Dissolve 4 Gms. of extract of opium in 5 mils. (or Cc.) of distilled water, add gradually, with constant stirring, 25 mils. (or Cc.) of distilled water, filter, and wash the filter

and residue with sufficient distilled water to make the solution measure exactly 50 mils. (or Cc.) From this point proceed as directed for the assay of opium on page 860, beginning with the words "Place in a small mortar, etc." As the morphine obtained represents 2 Gms. of the powdered extract of opium, the weight multiplied by 50 will express the percentage of anhydrous morphine in the extract.

Assay of Tincture of Opium and Tincture of Deodorized Opium.—Transfer 80 mils. (or Cc.) of tincture of opium or tincture of deodorized opium to an evaporating dish and evaporate it on a waterbath until the alcohol is all removed. As more or less precipitation will occur upon evaporation of the alcohol, the concentrated liquid should be decanted and filtered, and the residue thoroughly broken up with a glass rod and washed with successive portions of distilled water (the washings being passed through the first filter) until the filtrate passes colorless and tasteless; the filtrate and washings are then again evaporated until the weight is reduced to 40 Gms. From this point proceed as directed for the assay of opium on page 860, beginning with the words "Transfer the extract, etc." As the morphine obtained represents 40 mils. (or Cc.) of the respective tincture, the amount ascertained by calculation when multiplied by 2.5 will express the amount of anhydrous morphine in 100 mils. (or Cc.) of the tincture.

ASSAY OF PHYSOSTIGMA AND ITS PREPARATIONS.

The chief constituent of calabar bean is physostigmine, associated with three other alkaloids of minor importance. It is soluble in ether, as is also eseridine, which acts like physostigmine, but calabarine is insoluble in that liquid. Eseramine is devoid of physiological activity. The Pharmacopœia requires that physostigma shall contain not less than 0.15 per cent. of ether-soluble alkaloids; extract of physostigma, not less than 1.7 per cent. nor more than 2.3 per cent., and tincture of physostigma, not less than 0.013 Gm., nor more than 0.017 Gm. of ether-soluble alkaloids in 100 mils. (or Cc.).

Assay of Physostigma.—Transfer 15 Gms. of physostigma, in No. 60 powder, into a flask of 250 mils. (or Cc.) capacity and add 150 mils. (or Cc.) of ether; stopper the flask, shake it well and allow it to stand 10 minutes. Then add 10 mils. (or Cc.) of a 5 per cent. aqueous solution of sodium bicarbonate and shake the mixture vigorously at intervals during 4 hours. Now add 15 mils. (or Cc.) of distilled water, again shake the flask well, and, when the drug has settled, decant 100 mils. (or Cc.) of the ethereal solution, representing 10 Gms. of physostigma. Filter the solution through a small pledget of absorbent cotton into a beaker and rinse the graduated cylinder and cotton with ether. Add 20 mils. (or Cc.) of tenth-normal sulphuric acid and evaporate off the ether, stirring during the evaporation with a rubber-tipped glass rod. After the resinous and fatty matter has agglutinated,

pour off the acid solution through a wetted filter into a separator. Redissolve the residue in the beaker in about 15 mils. (or Cc.) of ether, add 2 mils. (or Cc.) of tenth-normal sulphuric acid, evaporate the ether with continued stirring as before and pour the acid solution on the filter. Repeat this operation until all of the alkaloid is extracted and then wash the filter with distilled water until it is free from alkaloids. Collect the solution and washings in a separator, add sufficient sodium bicarbonate to make the liquid decidedly alkaline to litmus and completely extract the alkaloids by shaking out with successive portions of ether. (Use 25, 15, 10 and 10 mils. (or Cc.) of ether, or more if necessary.) Wash the combined ether solutions with 10 mils. (or Cc.) of distilled water, separate the water completely, and filter the ether solution, washing the container and filter with ether. Evaporate the ether solution to dryness, dissolve the alkaloids from the residue in exactly 5 mils. (or Cc.) of tenth-normal sulphuric acid and titrate the excess of acid with fiftieth-normal potassium hydroxide solution, using cochineal test-solution as indicator. Each mil. of tenth-normal acid corresponds to 0.02752 Gm. of the ether-soluble alkaloids of physostigma. The weight of alkaloids obtained from the 10 Gms. of drug when multiplied by 10 will represent the percentage of ether-soluble alkaloids in the sample of physostigma examined.

Assay of Extract of Physostigma.—Introduce 3 Gms. of powdered extract of physostigma into a 250 mil. (or Cc.) flask, add 10 Gms. of washed sand and mix thoroughly. Then add 150 mils. (or Cc.) of ether and from this point proceed as directed for the assay of physostigma on page 862, beginning with the words "stopper the flask, etc." As 2 Gms. of the extract are represented in the final steps of the assay, the weight of ether-soluble alkaloids ascertained when multiplied by 50 will express the percentage of alkaloids in the extract.

Assay of Tincture of Physostigma.—Having evaporated 150 mils. (or Cc.) of tincture of physostigma on a waterbath to about 20 mils. (or Cc.), add 10 Gms. of purified sawdust (see page 841) to the liquid and incorporate it thoroughly. Continue the waterbath heat until the mixture is dry, then transfer the latter to a 250 mil. (or Cc.) flask and add 150 mils. (or Cc.) of ether. From this point proceed as directed for the assay of physostigma on page 862, beginning with the words "stopper the flask, etc." The amount of ether-soluble alkaloids obtained in the assay will represent the amount present in 100 mils. (or Cc.) of the tincture.

ASSAY OF PILOCARPUS AND ITS PREPARATIONS.

As our knowledge of the alkaloidal constituents of jaborandi leaves, with the exception of pilocarpine, is as yet not entirely satisfactory, the Pharmacopœia very properly recognizes the valuation of the

drug on the basis of total alkaloidal content as most desirable, and requires that pilocarpus shall contain not less than 0.6 per cent. of total alkaloids. This percentage represents fairly the average content of alkaloids in the leaves at the present time, for, while in the past inferior pilocarpus (running as low as 0.3 or 0.35 per cent. of alkaloids) has been met with occasionally, it has also been possible to procure some lots containing as much as 1 per cent. and over. In the assay of pilocarpus leaves it frequently happens that persistent emulsions occur, which are difficult to break up; the application of hot water to the exterior of the separator has been found to serve a good purpose. The Pharmacopœia requires that pilocarpus leaves shall contain, as already stated above, not less than 0.6 per cent. of total alkaloids, and the fluidextract of pilocarpus not less than 0.55 Gm., nor more than 0.65 Gm. of the same in 100 mils. (or Cc.).

Assay of Pilocarpus.—Introduce 15 Gms. of pilocarpus, in No. 60 powder, into a 250 mil. (or Cc.) flask, add 150 mils. (or Cc.) of chloroform and proceed as directed for the assay of belladonna root on page 846, beginning with the words "stopper the flask, etc." Instead of adding 25 mils. (or Cc.) of distilled water after maceration, as directed for belladonna root, add but 5 mils. (or Cc.), and when the drug has settled, withdraw 100 mils. (or Cc.) of the clear chloroform solution from the bottom of the flask, and finally dissolve the alkaloids from the residue in 8 mils. (or Cc.) of tenth-normal sulphuric acid instead of 5 mils. (or Cc.). Each mil. (or Cc.) of tenth-normal acid corresponds to 0.0208 Gm. of the total alkaloids of pilocarpus. The amount of alkaloids ascertained by calculation to be present in the residue, when multiplied by 10 will represent the percentage of total alkaloids in the drug.

Assay of Fluidextract of Pilocarpus.—Drop 15 mils. (or Cc.) of fluidextract of pilocarpus evenly from a pipette over the surface of 15 Gms. of purified sawdust (see page 841), and evaporate the mixture to dryness on a waterbath. Having transferred the dry mixture to a 250 mil. (or Cc.) flask, add 150 mils. (or Cc.) of chloroform and from this point proceed as directed for the assay of belladonna root on page 846, beginning at the words "stopper the flask, etc." Modify the directions given for the assay of belladonna root, by increasing the amount of ammonia water to 6 mils. (or Cc.) mixed with 5 mils. (or Cc.) of distilled water, which is to be used, in divided portions to rinse the dish in which the fluidextract and sawdust mixture was evaporated, the rinsings being added to the mixture in the flask. As in the case of the assay of pilocarpus, the 100 mils. (or Cc.) of chloroform must be drawn off from the bottom of the flask. As 10 mils. (or Cc.) of fluidextract of pilocarpus are represented in the final residue, the amount of alkaloids ascertained to be therein, when multiplied by 10 will express the amount present in 100 mils. (or Cc.).

CHAPTER LXII.

NEUTRAL PRINCIPLES AND GLUCOSIDES.

BESIDES organic acids and alkaloids, plants furnish a number of valuable principles which have a neutral reaction, and, for convenience, are divided into bitter principles and glucosides, the former being also known as amaroids. The distinguishing feature of the latter class is that when treated with diluted acids or ferments they split up into glucose, and a new body, differing from the original substance acted upon, but characteristic of that substance. With very few exceptions, glucosides do not contain nitrogen. Although glucosides are an important group of plant products, only two are officially recognized in the Pharmacopœia, partly due to the fact that they do not always constitute the active principle of the plant, and are in many cases associated with other bodies. A few glucosides appear to have a dual character, for, while yielding glucose by the treatment above mentioned, some also possess basic and others acid properties. As stated in a previous chapter, both glucosides and bitter principles are distinguished from alkaloids by the ending *in* or *inum*.

The following official neutral principles are used by physicians to a greater or less extent: Aloin, chrysarobin, elaterin, glycyrrhizin, salicin, santonin, and strophanthin; of these, salicin and strophanthin are true glucosides.

Aloin.—The name aloin is used, both commercially and in the Pharmacopœia, to designate the neutral, bitter, crystalline principle of aloes, irrespective of the source, and more specifically defined as a pentoside or mixture of pentosides, varying in chemical composition and properties. (The name pentoside is used to designate a class of carbohydrates capable of yielding upon hydrolysis with diluted acids, pentoses or sugars having 5 carbon atoms, such as arabinose, xylose, etc., see page 720.)

It is more than probable that a very large proportion of the aloin sold in this country is derived from Curaçao aloes, as this variety is much richer in aloin than either Barbadoes or Socotra aloes, and, moreover, comparatively little of the latter variety reaches this market. Cape aloes, which was formerly supposed not to contain any crystalline aloin, has been shown to contain the same, and the name capaloin has been given to it. Tschirch in 1898 succeeded in crystallizing capaloin from alcohol and ether in the form of colorless needles.

Various methods have been proposed for the manufacture of aloin, the best known of which is the treatment of aloes with hot water acidulated with either hydrochloric or sulphuric acid; after the infusion has been allowed to stand for a day it is carefully decanted from sediment, concentrated at a moderate temperature, preferably in a vacuum apparatus, and set aside in a cold place, when crystals or crystalline crusts of aloin will separate. The aloin may then be purified by means of filter presses and recrystallization from hot water or very dilute alcohol. The addition of a little acid has been found advantageous in avoiding the contamination of aloin with non-crystallizable matter, which is less soluble in acidulated water than in plain water.

A more recent method suggested by Schaefer depends upon the property of aloin of forming very difficultly soluble compounds with the alkaline earths in ammoniacal solution, which, upon decomposition with an acid, yield aloin. The following method for determining the aloin content in aloes indicates a process of manufacture for aloin on a large scale: 50 Gms. of aloes are mixed with 300 mils. (or Cc.) of hot water, with the addition of a few drops of hydrochloric acid. On cooling the solution is decanted from the separated resin, mixed rapidly with 50 mils. (or Cc.) of 20 per cent. ammonia water and a solution of 15 Gms. of calcium chloride in 30 mils. (or Cc.) of water. The precipitate is collected after fifteen minutes, the water expressed, and the lime salt decomposed by triturating it in a mortar with a slight excess of hydrochloric acid. The resulting mixture of aloin and calcium chloride is then dissolved in a small quantity of hot water, filtered, the filter washed with hot water, and the aloin crystallized out at a low temperature with the aid of ice. As much as 30 per cent. of aloin in fine, light-yellow crystals has been obtained from commercial aloes by this method.

The average yield of aloin from the different commercial varieties of aloes varies from 4 to 20 per cent. and over.

Aloin is supposed to owe its value as a laxative to a substance known as emodin, with which it is associated in aloes and into which it is in all probability converted by the alkaline intestinal fluids. If aloin be treated with ether, any emodin present will be extracted, aloin being insoluble in ether. The peculiar color reactions, from orange to deep cherry red, observed when 5 per cent. ammonia water is shaken with an ethereal extract, obtained from a decoction of aloes by agitation with ether, are due to emodin; pure aloin, freed from emodin, fails to show these colors. This is known as Borntræger's reaction and is practically identical with the official test for the limit of emodin, except that benzene is used in the latter in place of ether for solution of the emodin.

Aloin of commerce is sometimes contaminated with resinous and other matter, which can be detected by imperfect solubility of the sample in cold water. Aloin obtained from Curaçao aloes dissolves

in nitric acid with a cherry-red color, which distinguishes it from capaloin, nataloin, and socaloin. It may also be distinguished from the two first named by acquiring a red color by Klunge's test with copper sulphate and concentrated solution of sodium chloride; upon addition of alcohol the red color changes to violet. According to Tschirch this reaction depends upon the presence of a small percentage of isobarbaloin, and the red color will be intensified if a small quantity of hydrocyanic acid be used in place of the sodium chloride.

Chrysarobin.—This mixture of neutral principles, derived from Goa Powder by treatment with hot benzene, has been at times confounded in commerce with chrysophanic acid. As thus obtained it is still contaminated with some impurities, but corresponds in general to the requirements of the Pharmacopœia; it can be obtained pure, in the form of small yellow scales, by repeated crystallization from acetic acid, and then has the composition $C_{30}H_{26}O_7$. Although the Pharmacopœia states that 1 Gm. chrysarobin is soluble in 12.5 mils. (or Cc.) of chloroform, the commercial article frequently fails to respond to this test. The following test of the Pharmacopœia may be used to distinguish chrysarobin from chrysophanic acid, the former acquiring a violet-red color, while the latter produces a yellow-colored liquid: Mix 0.001 Gm. of the substance with 2 drops of fuming nitric acid and add to the red-colored mixture a few drops of ammonia water.

Elaterin. $C_{20}H_{28}O_5$.—Commercial elaterium owes its medicinal virtues to a neutral principle called elaterin, which may be extracted by treatment with chloroform and subsequent addition of ether to the chloroformic solution, whereby crystals of elaterin are precipitated, being but slightly soluble (about 1 grain in 1 fluidounce) in ether. The crystals may be further purified by washing them with a little ether and recrystallizing from chloroform. The yield of elaterin varies from 25 to 35 per cent. of the weight of elaterium, and the two substances must not be confounded with each other.

Glycyrrhizin.—This substance, although for a long time considered to be a neutral principle and also a glucoside, is now looked upon as a tribasic acid, *glycyrrhizic acid*, having the composition $C_{44}H_{63}O_{18}N$, which exists in licorice root in combination with ammonia as an acid salt. It possesses no medicinal properties, and is valuable only on account of its very sweet taste. It is recognized in the Pharmacopœia in combination with ammonia as *ammoniated glycyrrhizin*, and in the process for the preparation of this compound the complete extraction of glycyrrhizin from the drug is effected by adding ammonia water to the menstruum, so that a neutral ammonium glycyrrhizate may be formed. The addition of sulphuric acid to the percolate causes the precipitation of the glycyrrhizin, which, for the purpose of purification, is collected, redissolved in ammonia water, and again precipitated,

being finally dissolved in sufficient ammonia water and obtained in scales by spreading the solution on glass and drying. When boiled with diluted sulphuric acid pure glycyrrhizin splits up into glycyrrhetin, $C_{32}H_{47}O_4N$, and parasaccharic acid, $C_6H_{10}O_8$, which latter reduces Fehling's Solution like glucose, and thus gave rise to the former view that glycerrhizin was a glucoside.

Salicin. $C_{13}H_{18}O_7$.—Several methods are in use for the extraction of this principle from willow and poplar barks. The bark may be macerated and boiled with milk of lime, the decoction, after straining, being allowed to subside; the clear liquid is concentrated, treated with animal charcoal and evaporated to dryness, after which the residue is exhausted with weak alcohol, from which the salicin will crystallize after removal of the alcohol by distillation. Another plan is to exhaust the bark with boiling water and deprive the decoction of coloring matter and tannin by digestion with litharge or treatment with basic lead acetate; any free acid present in the liquid is neutralized with chalk. The filtrate, on concentration, will yield crystals of salicin, which may be purified by recrystallization.

When boiled with diluted sulphuric acid, salicin takes up water and splits up into glucose and saligenin or salicyl alcohol, thus, $C_{13}H_{18}O_7 + H_2O = C_6H_{12}O_6 + C_7H_8O_2$.

A characteristic reaction of salicin is the production of a bright red color when the substance is dissolved in concentrated sulphuric acid, the color disappearing upon the addition of water. The production of the fragrant odor of the oil of meadow sweet when salicin is heated with diluted sulphuric acid and potassium dichromate also serves to distinguish this substance from others; the odor is due to the formation of salicylic aldehyde.

Santonin. $C_{15}H_{18}O_3$.—Chemically santonin is the anhydride of a weak acid, although generally looked upon as a neutral substance. It is obtained by mixing crushed santonica (the dried unexpanded flower heads of *Artemisia pauciflora*) with slaked lime and exhausting the mixture with hot water; the resulting solution of calcium santoninate is concentrated and decomposed with hydrochloric acid. The crude santonin is treated with diluted ammonia water, dissolved in alcohol, and the solution decolorized with bone-black, after which it is allowed to crystallize.

Santonin possesses the property of turning yellow when exposed to the light, and then forms a yellow solution with alcohol, from which, however, it again crystallizes colorless.

The following may be mentioned as characteristic reactions of santonin: a red color is produced when 0.5 Gm. of santonin is heated with 5 mils. (or Cc.) of an alcoholic solution of potassium hydroxide; if 0.010 Gm. of santonin be added to a mixture of 1 mil. (or Cc.) each of sulphuric acid and water a colorless solution is obtained, which,

when heated to 100° C. (212° F.) assumes a violet color upon addition of one drop of very dilute ferric chloride solution.

Strophanthin.—The Pharmacopœia defines the official strophanthin to be a glucoside or mixture of glucosides obtained from the seed of *Strophanthus Kombé.* Considerable confusion and uncertainty exist regarding the character of the strophanthin obtained from different species of strophanthus, and the various data published by different authors must be accepted tentatively, at least for the present.

Strophanthin may be extracted from finely powdered seed which has been previously deprived of fat by treatment with ether or petroleum benzin, with 70 per cent. alcohol. The tincture thus obtained is distilled to free it from alcohol, and the residue dissolved in water and filtered. After addition of tannic acid to the filtrate, the resulting precipitate is washed, mixed with lead oxide, dried and extracted with alcohol. The addition of ether to the alcoholic solution causes the precipitation of strophanthin.

The glucosidal character of strophanthin is shown by heating it with diluted hydrochloric acid, when strophanthidin is formed, and a sugar which reduces Fehling's Solution. Strophanthin is extremely toxic and is soluble in water and in alcohol. By heating strophanthin with dilute mineral acids, various shades of green color, changing to violet or blue, are produced, and are more or less characteristic.

Careful review by H. Thoms (1904), of the work previously done by others on the constituents of strophanthus, has shown that strophanthin obtained from the Kombé variety of seed contains small proportions of nitrogen, which were traced to the presence of choline and trigonelline, the latter alkaloids having been also found in the seed of the same variety. Strophanthin from the seed of strophanthus hispidus is free from nitrogen, but not capable of crystallization. The same author succeeded in obtaining 3.6 per cent. of crystalline strophanthin, also free from nitrogen, from the seed of strophanthus gratus, which after recrystallization was found to have the composition indicated by the formula $C_{30}H_{46}O_{12} + 9H_2O$. In view of the preceding statements it would seem desirable to indicate the different varieties of strophanthin according to their source, and to recognize officially the glucoside from strophanthus gratus, which has been found to possess a high therapeutic value.

Among the reagents mentioned in the Pharmacopœia in connection with the standardization of digitalis, squill and strophanthus by biological methods is the glucoside *Ouabain,* which occurs in different plants and may be obtained from the seed of strophanthus gratus. The chemical composition of ouabain is represented by the empirical formula $C_{30}H_{46}O_{12} + 9H_2O$. It is met with in the form of colorless, quadratic crystals, having a bitter taste, easily soluble in hot water, soluble in 100 parts of cold water and in about 30 parts of cold dehy-

drated alcohol. When heated with diluted hydrochloric acid, ouabain takes up the elements of water and yields rhamnose, $C_6H_{12}O_5$, and a resinous substance.

Closely allied to the glucosides and neutral principles is a class of plant products, not used medicinally in a separate state, but comprising the active constituents of a number of drugs, and known by the general group name.

Saponins.—The first use of the name saponin occurred in connection with the saponaceous constituent of the root of saponaria rubra, discovered in 1808 by Schrader. While formerly the view prevailed that the peculiar substance called saponin, as found in different plants, is identical, careful investigation of the subject by R. Kobert and his associates and pupils has demonstrated the fact that the name saponin should be applied to a group of plant constituents having certain chemical and physical properties in common, yet differing in constitution, physiological effect, etc.[1]

Although saponins are met with in several hundred plants, both monocotyledons and dicotyledons, distributed among 46 or more families, practically nothing is known regarding the important part they may play in plant physiology. They occur in all parts of plants; thus in the root of sarsaparilla, saponaria, senega, and helonias (chamælirium), the bulb of cyclamen, the bark of quillaja and guaiacum, the fruit of sapindus, the seed of æsculus, entada, and agrostemma, the stem of dulcamara, and the leaves of digitalis and guaiacum. Kobert inclines to the view that the saponins are formed in the leaves and deposited later in other parts of the plant.

One of the chief characteristics of the saponins, to which they owe their group name, is the property of forming aqueous solutions which foam strongly upon agitation, like solutions of soap, even when very dilute (1 in 10,000). The bubbles of froth, which in some cases are quite persistent, are destroyed if alcohol or ether be allowed to drop upon them. Another common property is the ability to hold fatty and resinous substances, when in a finely divided state, in perfect suspension in aqueous mixtures, thus producing emulsions of great stability. Finely divided vegetable substances are also kept in suspension in watery fluids by the presence of saponins. With few exceptions the saponins are readily soluble in water (all are soluble if the water be made slightly alkaline), and also in diluted alcohol, preferably if warmed. Some are soluble in cold absolute alcohol, but thus far none has been found soluble in ether, benzene, or carbon disulphide. A few dissolve with difficulty in chloroform. Many,

[1] Due acknowledgement is hereby made of the very interesting and valuable publication by Professor R. Kobert, of Rostock, Germany, entitled "Beiträge zur Kenntniss der Saponin Substanzen" (Contributions to our Knowledge of the Saponins), from which this brief abstract has been made.

but not all, saponins are precipitated from their solutions by addition of a saturated solution of ammonium sulphate, and this fact has been utilized as a means of separation. In some instances precipitation occurs in the cold, immediately or after the lapse of some time, while in others the application of heat is necessary, especially in weaker solutions. By this method it has been possible to separate polygalic acid from senegin in a decoction of senega, quillajic acid from quillajasapotoxin in a decoction of soap bark, and saporubric acid from saporubrin. The sapotoxin present in Levant soapwort, saponaria alba, which is precipitated by ammonium sulphate, has thus been shown not to be identical with the sapotoxin in quillaja.

All saponins have glucosidal properties, and are hydrolyzed when their solutions are heated with dilute mineral acids, being split up into dextrose and a non-toxic body, soluble in cold water, called sapogenin. The latter body, which is not identical for all saponins, has acid properties and forms water-soluble crystallizable salts with the alkalies. Some saponins are precipitated by neutral lead acetate others by basic lead acetate, and still others are affected by both reagents. Those precipitated by neutral lead acetate show an acid character toward litmus and Congo-red, and are designated as acids; thus, melanthinic acid, polygalic acid, quillajic acid, etc. The other saponins are neutral, some being known as sapotoxins, while others have been given specific names, such as assamin, chamælirin, senegin, etc. One drug, at least, is known to contain 3 neutral saponins—namely, sarsaparilla, the same being named parillin, sarsasaponin, and smilasaponin.

As a rule, saponins are amorphous bodies, but parillin and sarsasaponin are crystalline. They are characterized by a bitterish, acrid taste, sometimes accompanied by a burning sensation, and in fine powder are intensely irritating and sternutatory. With few exceptions saponins are decidedly toxic and have a solvent effect on red blood corpuscles. This poisonous property prevents their use in pharmacy in many cases, where their property of permanently suspending oils and resinous matter would otherwise make it very desirable. The saponin obtained from the root of helonias dioica, and known as chamælirin, is said to have been used at times for codliver oil emulsions because less toxic than the saponins of quillaja bark; but inasmuch as the saponins present in guaiacum bark and leaves have been found almost entirely devoid of toxic properties, these would naturally seem preferable to all others for emulsifying purposes.

The following color reactions observed by Kobert are worthy of special note: A characteristic red coloration occurs with many saponins if they are mixed with concentrated sulphuric acid and exposed to the air for some time, or carefully warmed. With an alcoholic solution of sulphuric acid, to which a drop of dilute solution of ferric chloride has been added, a greenish-blue coloration is produced, which reaction is useful for detection of saponins in microscopic sections of

vegetable drugs. A solution of selenous acid in concentrated sulphuric acid (Mecke's reagent) produces a cherry-red color with the acid saponin of cereus grandiflorus and other saponins, while a beautiful violet color is produced with guaiac-saponic acid. A very delicate reaction, resulting in an intense red color, is produced by adding to soapbark saponins some Millon's reagent as modified by Nasse (a solution of mercuric acetate to which a drop of potassium nitrite solution has been added just before using), and warming. Kobert states that this last reaction is useful for detection of quillaja preparations in oil emulsions.

Two general formulas have been proposed to represent the composition of the saponins, $C_nH_{2n-10}O_{18}$ by Flückiger, and $C_nH_{2n-8}O_{10}$ by Kobert, to one of which nearly all known saponins may be referred. To the first group belong quillajic acid, $C_{33}H_{56}O_{18}$, chamælirin, $C_{36}H_{62}O_{18}$, parillin (Flückiger), $C_{40}H_{70}O_{18}$, digitonin, $C_{33}H_{56}O_{18}$, sarsasaponin, $C_{40}H_{70}O_{18}$, and others, while quillajasapotoxin, $C_{17}H_{26}O_{10}$, melanthinic acid, $C_{29}H_{50}O_{10}$, senegin, $C_{18}H_{28}O_{10}$, smilasaponin, $C_{20}H_{32}O_{10}$, polygalic acid, $C_{19}H_{30}O_{10}$, and the acid and neutral saponins of guaiacum bark, $C_{21}H_{34}O_{10}$ and $C_{22}H_{36}O_{10}$, are members of the second group.

Inasmuch as the saponins are capable of forming insoluble lead compounds, Kobert recommends the following method for their extraction: To the concentrated decoction or tincture of the drug, solution of lead acetate is added; the resulting precipitate, after filtration, is mixed with some alcohol, treated with hydrogen sulphide, and again filtered. The residue is boiled with several portions of alcohol, the solutions added to the filtrate, and the whole evaporated to a syrupy consistence. Upon addition of ether to the cooled liquid, the saponins are precipitated. In order to recover any saponin not precipitable by lead acetate, solution of basic lead acetate should be added to the original filtrate, and the process then continued exactly as directed for the treatment of the precipitate obtained with neutral lead acetate.

The process of salting out by means of ammonium sulphate may also be employed for precipitation and separation of saponins in place of the lead acetate method mentioned above.

CHAPTER LXIII.

ANIMAL PRODUCTS USED IN PHARMACY.

BESIDES the well known animal ferments, pancreatin and pepsin, long since introduced into medicine as valuable digestive aids, the Pharmacopœia gives official recognition to several antitoxins of great value, and two very important glands of the animal body. As the pharmacist is occasionally called upon to handle these products, it is deemed proper to give them more than a passing notice.

Antidiphtheric Serum or Diphtheria Antitoxin.—The Pharmacopœia defines this preparation to be a fluid, having a potency of not less than 250 antitoxic units per mil. (or Cc.), separated from the coagulated blood of a horse, or other large domestic animal, which has been properly immunized against diphtheric toxin, and directs that it should be kept in sealed glass containers, in a dark place, at a temperature between 4.5° and 15° C. (40° and 59° F.).

Although large quantities of antidiphtheric serum are now manufactured in this country, foreign products, both in the dry and liquid form, are also imported.

The preparation of antidiphtheric serum can only be conducted at large establishments, especially designed for that purpose, and involves three distinct steps—namely, the preparation of the toxin or diphtheric poison to be injected into the horse, the immunization of the animal, and the preparation of the antitoxin or serum officially recognized. A full and interesting account of the process may be found in the *National Standard Dispensary*, 1916, pages 207–219.

Antidiphtheric serum is a yellowish or yellowish-brown, transparent or slightly turbid liquid, which is either odorless or has a slight odor, due to the addition of some antiseptic or preservative. It gradually loses its power, the loss varying between 10 and 30 per cent. in one year. The Pharmacopœia requires that it must be sterile and free from toxins, must not contain more than 0.5 per cent. of phenol or cresol, when either of these is used, and must not contain more than 20 per cent. of solids.

Only such sera may be sold as have been prepared and propagated in establishments licensed by the Secretary of the Treasury of the United States. The law requires that each container of serum sold by licensed establishments shall bear upon the label, in addition to the name of the serum, the name, address and license number of the manufacturer, and the date beyond which the contents cannot be expected to yield its specific results. The label must also contain the

laboratory number of the serum, the name and the percentage by volume of the antiseptic used (if any) and the total number of antitoxic units claimed for the contents of the container. The standard of strength, expressed in units of antitoxic power, shall be that established by the United States Public Health Service.

An antitoxic or immunity unit may be defined as the amount of antitoxin which will neutralize 100 times the minimum fatal dose of a test toxin when the two are mixed together and immediately injected subcutaneously into a standard-test guinea-pig of 250 Gms. body weight.

Under an act of Congress, approved July 1, 1902, and the regulations framed thereunder, the Director of the Hygienic Laboratory is required to examine all antitoxins for purity and potency. From time to time purchases of antidiphtheric serum are made in the open market by government officials, and these are carefully examined. If found not to conform to the prescribed requirements, the manufacturer is notified and steps are taken to insure the withdrawal of that particular lot from sale. Not only is the serum tested for its potency, but great care is taken to determine its freedom from contamination by foreign bacteria, and finally to insure the absence of chemical poisons, especially tetanus toxin.

Purified Antidiphtheric Serum.—This purified product represents a solution of certain antitoxic substances in a solution of sodium chloride. It is obtained by separating the antitoxin-bearing globulins contained in the serum or plasma from immunized animals from the other constituents, and dissolving them in water; sufficient sodium chloride is then added to make a solution containing from 0.6 to 0.9 per cent. of salt.

The purified serum has the same potency and properties as the antidiphtheric serum mentioned above, and like it must be preserved in a dark place in sealed glass containers at a low temperature. The Pharmacopœia gives the following synonyms for this serum: *Antidiphtheric Globulins, Concentrated Diphtheria Antitoxin, Diphtheric Antitoxin Globulins, Refined* and *Concentrated Diphtheria Antitoxin.*

Dried Antidiphtheric Serum, also known as *Dried Diphtheria Antitoxin.*—This highly concentrated antitoxin is prepared by careful evaporation of either of the above mentioned sera in a vacuum apparatus over sulphuric acid or other desiccating agent, or by passing over it a current of warm air freed from bacteria. It has a potency of not less than 4000 units per gram and must be preserved in hermetically sealed amber-colored glass containers free from air, at a temperature between 4.5° and 15° C.

Dried diphtheria antitoxin occurs either as orange or yellowish flakes, or in small lumps, or as a yellowish-white, odorless powder.

It is soluble in 9 parts of distilled water, and must comply with all the requirements for control and labeling mentioned above under Antidiphtheric Serum. The dried serum, if properly kept, does not lose in potency as does the liquid serum.

Antitetanic Serum, also known as *Tetanus Antitoxin.*—The Pharmacopœia defines this product as a fluid, having a potency of not less than 100 units per mil. (or Cc.) separated from the coagulated blood of a horse or other large domestic animal, which has been properly immunized against tetanus toxin. It must be preserved in sealed glass containers in a dark place at a temperature between 4.5° and 15° C.

Antitetanic serum occurs as a yellowish or yellowish-brown transparent or slightly turbid liquid with sometimes a slight granular deposit, nearly odorless, or having an odor due to the presence of the antiseptic used as a preservative. It gradually loses its potency, the loss being greater at higher temperatures than at lower. The serum must be sterile; must be free from toxins or other bacterial products; and must not contain an excessive amount of preservative (0.5 per cent. of phenol or cresol, when either of these is used); and the total solids must not exceed 20 per cent. Serum of a lower potency than 100 units per mil. must not be sold or dispensed. Only such sera may be sold or dispensed as have been prepared and propagated in establishments licensed by the Secretary of the Treasury of the United States.

The law requires that each container of serum sold or dispensed by licensed establishments shall bear upon the label, in addition to the name of the serum, the name, address and license number of the manufacturer and the date beyond which the product cannot be expected to yield its specific results. The label must also contain the laboratory number of the serum, and the total number of antitoxic units claimed for the contents of the container.

Purified Antitetanic Serum.—As in the case of purified diphtheria antitoxin, this serum is obtained by separating the antitoxin-bearing substances from the other constituents of the serum or plasma of the horse, or other large domestic animal, properly immunized against tetanus toxin, and dissolving these in water and adding sufficient sodium chloride to make a solution containing from 0.6 to 0.9 per cent. of salt.

The purified serum has the same potency and properties as the antitetanic serum mentioned above, and like it must be preserved in a dark place in sealed glass containers at a low temperature. The Pharmacopœia gives the following synonyms for this serum: *Antitetanic Globulins, Concentrated Tetanus Antitoxin, Refined* and *Concentrated Tetanus Antitoxin, Tetanus Antitoxin Globulins.*

Dried Antitetanic Serum, also known as *Dried Tetanus Antitoxin.*—This concentrated product may be obtained by careful evaporation

of either antitetanic serum or the purified serum, in a vacuum apparatus over sulphuric acid or other desiccating agent, or by passing a current of warm air freed from bacteria over it. It has a potency of not less than 1000 units per gram and must be preserved in hermetically sealed amber-colored glass containers, free from air, at a temperature between 4.5° and 15° C.

Dried tetanus antitoxin occurs either as orange or yellowish flakes, or in small lumps, or as a yellowish-white, odorless powder. It is soluble in 9 parts of distilled water, and must comply with the requirements for control and labeling mentioned under Antitetanic Serum. The dried serum, if properly kept, does not lose potency, as does the liquid serum.

Dried Suprarenals, also known as *Desiccated or Dried Suprarenal Glands.*—This preparation, to which the Pharmacopœia applies the Latin name *Suprarenalum Siccum,* is officially defined to be the suprarenal glands of animals which are used as food by man, cleaned, dried, freed from fat, and powdered, and containing not less than 0.4 per cent. nor more than 0.6 per cent. of epinephrine, the active principle of the gland.

The suprarenal capsule is situated above each kidney, and consists of an external cortex of peculiarly arranged cells derived from the meosoblast, and an internal medulla composed of cells derived originally from the sympathetic ganglia. The cortex is apparently without medicinal value, the important physiological properties residing in the medulla.

After removal of the external fat and connective tissue the glands are dried as rapidly as possible in a current of warm air at a moderate temperature, and, when sufficiently dry, are reduced to coarse powder, and the remaining fat removed by treatment with petroleum benzin. It is important that all moisture be removed, by exposure in a desiccator if necessary, in order to avoid subsequent putrefaction, after which the residue may be reduced to fine powder, and should be preserved in closely stoppered bottles.

Desiccated suprarenal glands occur as a light, yellowish-brown, amorphous powder, having a slight, characteristic odor, and partly soluble in water; 1 part represents approximately 6 parts of fresh glands, free from fat. The Pharmacopœia requires that the powder shall not contain more than 7 per cent. of moisture and shall yield upon incineration not more than 7 per cent. of ash. If 0.5 Gm. of desiccated suprarenal glands be macerated with 25 mils. (or Cc.) of water for fifteen minutes and filtered, the filtrate should give an emerald-green color upon the addition of a few drops of ferric chloride test-solution. The green color disappears quite rapidly.

The active principle of the suprarenal glands has been isolated and found to be a basic substance, capable of combining with acids to form difficultly or non-crystallizable salts. It has been named

epinephrine and adrenalin by different investigators, and occurs on the market as a light grayish or brownish-white microcrystalline powder and also in the form of a solution of its chloride of $\frac{1}{10}$ per cent. strength. Its action is that of a powerful vasoconstrictor causing a marked rise of arterial blood-pressure, when injected intravenously.

The determination of the active principle of dried suprarenals is directed to be made colorimetrically, and since the color tint obtained from different samples may vary from yellowish pink to bluish pink, the preparation of standard color solutions corresponding to these limits is necessary. The Pharmacopœia directs the use of mixtures of various quantities of cobaltous chloride test-solution and gold chloride test-solution for the purpose of comparison. The percentage of epinephrine indicated by the official color standards is based on the treatment of 0.01 Gm. of dried suprarenals in 10 mils. (or Cc.) of distilled water with 0.005 Gm. of finely powdered manganese dioxide, the mixture being thoroughly shaken during 1 hour and then filtered; the color of the filtrate is then compared in a test tube with the color of the standard solutions.

Dried Thyroids, also known as *Desiccated Thyroid Glands.*—The Pharmacopœia applies the Latin name *Thyroideum Siccum* to this preparation, and defines it to consist of the thyroid glands of animals which are used as food by man, freed from connective tissue and fat, dried and powdered, and containing not less than 0.17 per cent., nor more than 0.23 per cent. of iodine in thyroid combination.

The thyroid gland is a very vascular organ, situated in front and on either side of the trachea or upper windpipe. It consists of two lobes connected at their upper extremities by a bridge of pale-colored tissue. When freed from all external fat and connective tissue the lobes are broadly almond-shaped, and consist of a firm, succulent mass of tissue with dark red color.

The preparation of powdered thyroid glands is practically the same process as mentioned in the preceding article for dried suprarenal glands, and, like these, the powder must be preserved in well stoppered bottles to avoid absorption of moisture and subsequent deterioration.

Desiccated thyroid glands constitute a yellowish amorphous powder, having a slight peculiar odor. One part of dried thyroids represents approximately 5 parts of the fresh glands and contains not more than 6 per cent. of moisture; upon incineration it should not yield more than 5 per cent. of ash. Small proportions of iodine are present in the form of organic compounds, as shown by the official test, but iodides, added fraudulently, may be detected by treating a cold extract of the powder with sodium nitrite, and, after acidulating with nitric acid, shaking with chloroform, when the latter should not assume the characteristic violet color of iodine.

The Pharmacopœia directs that the iodine present in thyroid combination be determined by first converting it into alkali iodate and perhaps some iodide, by fusion with potassium carbonate, sodium carbonate and potassium nitrate; after solution of the residue, treatment with chlorinated soda solution in excess and phosphoric acid converts all iodide into iodate, and prolonged boiling insures the elimination of all products that might act on the potassium iodide solution to be added later. Phosphoric acid is used because it is nonvolatile in the boiling solution. When potassium iodide solution is added to the cooled liquid, iodine will be liberated in proportion to the amount of iodate present and obtained from the thyroids, thus: $5KI + KIO_3 = 3K_2O + I_6$. As shown by the equation, only one-sixth of the total iodine liberated comes from the dried thyroids and hence, while 1 mil. (or Cc.) of two-hundredth-normal sodium thiosulphate solution corresponds to 0.0006348 Gm. of iodine, only one-sixth of that amount, or 0.0001058 Gm. can be considered as coming from the thyroids. The percentage of iodine present in the sample of dried thyroids is ascertained by multiplying the number of mils. (or Cc.) of the sodium thiosulphate solution required by 0.01058 (0.0001058×100), since 1 Gm. of the dried glands is used for the assay.

Digestive Ferments.—It is well known that the digestion of food is of a twofold character; one takes place after the food has entered the stomach, and is called gastric or peptic digestion, the other occurring after the partly digested food leaves the stomach, is known as pancreatic or intestinal digestion. During the mastication of food it becomes mixed with the secretion of the salivary glands, which contains a substance known as *ptyalin*, belonging to the class of unorganized ferments usually termed enzymes by physiologists, from the Greek word *enzymos*, meaning fermented. The special action of ptyalin appears to be to prepare starchy food for subsequent digestion, as it is capable of converting starch into dextrose; in the presence of hydrochloric acid even as weak as 0.4 per cent., it is rendered inert, being most active in slightly alkaline liquids.

The action of ferments upon food depends upon the character of the latter, as the different ferments have specific functions and cannot be used indiscriminately for all kinds of food. Food partaken of by animals is either albuminoid or amylaceous in its nature, the former being converted into peptones, the latter into sugars. The digestive action of ferments on albuminoids is called the proteolytic action, from the word *proteolysis*, meaning the change occurring in proteids while being digested; the digestion of amylaceous food, on the other hand, is known as the amylolytic action of ferments, from *amylolysis*, meaning the conversion of starch into sugar.

The various products formed during the digestion of food are syntonin, albumoses, and peptones. The first, also known as acid

albumin, is probably produced by the action of hydrochloric acid (of which gastric juice contains from 0.1 to 0.25 per cent.) on albuminoid substances, and occurs soon after the ingestion of food. After peptic digestion has set in albumoses are formed, which are gradually converted into peptones, the end-products of digestion and the form in which albuminoid food is assimilated, peptones being readily diffusible and absorbed by a process of dialysis. As stated before, digestion is not completed in the stomach; the mixture of albumoses and peptones, forming a smooth, pulpy mass called chyme, passes into the intestines, where the conversion into peptones and other diffusible products is completed.

Pancreatin and pepsin are the two agents secreted in the body of all animals, without which assimilation of food would be impossible; both are recognized in the Pharmacopœia and are exceedingly interesting products.

Pancreatin.—By this name is recognized a mixture of enzymes found in the pancreatic juice, the secretion of a gland known as the pancreas, situated in the epigastric and hypochondrial regions beneath the stomach and in part next to the duodenum, with which it is connected by means of a small duct. The pancreatic juice is a clear, colorless, somewhat viscid liquid of an alkaline reaction, without odor and of an insipid, somewhat saline taste; it possesses both proteolytic and amylolytic activity, besides being capable of emulsifying fatty matter.

The Pharmacopœia gives no directions for the preparation of pancreatin, and different manufacturers probably pursue different methods. The following was suggested in the first edition of the *National Formulary:* Fresh pancreas of the hog, freed as much as possible from fat and adhering membranes, is reduced to a fine paste by means of a suitable mincing-machine; it is next mixed with half its weight of cold water and kneaded thoroughly and frequently during one hour, after which the mass is transferred to a strainer and forcibly expressed; the liquid is filtered as quickly as possible through flannel, and to the filtrate is added an equal volume of alcohol; the precipitate is collected, drained, and freed by pressure from as much of the adherent liquid as possible; it is then spread on shallow trays, dried by exposure to warm air at a temperature not exceeding 40° C. (104° F.) and reduced to powder. When large quantities of pancreas are operated upon it is advisable to use water saturated with chloroform, which will retard decomposition for a long time.

In some instances the finely mixed pancreas is macerated with highly diluted hydrochloric acid, in place of plain water, and the fat is often removed from the powdered mass by means of purified benzin.

Pancreatin consists of a mixture of at least 4 soluble unorganized ferments, more specifically termed enzymes, and differing from one

another in their digestive functions. They are designated respectively as the proteolytic, the amylolytic or diastasic, the fat-splitting, and the milk-curdling ferment. As yet none of the enzymes has been isolated in a pure state. These enzymes do not exist as such in the cells of the pancreas, but are derived from the zymogens during the digestive process.

Trypsin, the proteolytic enzyme, resembles pepsin in its behavior toward albuminoids, and continues in the intestines the work of that ferment begun in the stomach. It differs, however, from pepsin in acting best in a slightly alkaline medium and in splitting the products of peptic digestion, the albumoses and peptones, into simpler bodies, better adapted for absorption as nutritive agents. It is particularly active toward fibrin and muscular tissue, but does not digest coagulated egg albumen as rapidly as pepsin. It also rapidly digests the casein of milk, with the intermediate formation of metacasein, coagulable by boiling. The presence of a small amount of sodium or potassium bicarbonate in the milk prevents the coagulation of the metacasein. As in the case of pepsin, the action of trypsin is confined to the surface of the substance exposed, the more soluble bodies passing into solution as fast as formed.

While the presence of about 1 per cent. of sodium carbonate or bicarbonate, of the digesting mass, is favorable to increased tryptic activity, the latter also occurs in neutral or even very slightly acid media, showing that the presence of alkali is not absolutely essential. The presence of very small proportions of acid (about 0.03 per cent. of hydrochloric or 0.25 per cent. of acetic acid) is by no means hurtful to the action of trypsin, but an increase to even as little as 0.1 per cent. of hydrochloric acid completely destroys the ferment, and hence its activity ceases at once in a medium having the degree of acidity favorable to peptic action. Trypsin is most active at a temperature between 37° and 40° C. (98.6° and 104° F.), and continues up to 50° C. (122° F.), above which it rapidly diminishes, and ceases altogether at 75° C. (167° F.).

Amylopsin, or pancreatic diastase, closely resembles ptyalin and grain diastase, both in properties and products of conversion, but its action is much more energetic, rapidly liquefying starch paste and converting starch into dextrin and maltose. Its greatest activity is manifested at a temperature between 30° and 45° C. (86° and 113° F.), and is destroyed at 65° C. (149° F.). The action of amylopsin is not increased by alkalies and is weakened by the presence of acids.

Steapsin, or lipase, has the special function of emulsifying fats and splitting them up into glycerin and free fatty acids. It is rapidly destroyed by strong alcohol and by all acids, except the fatty, being the most delicate of the pancreatin enzymes. Its action on fats can be readily demonstrated by adding a few drops of a neutral solution of pancreatin to a neutral ethereal solution of butter, when upon

addition of a little litmus solution the characteristic color-change will take place.

Rennin, or the milk-curdling ferment, is probably identical with that found in the stomach.

The Pharmacopœia describes pancreatin as a cream-colored amorphous powder, possessing at most only a faint peculiar but not offensive odor; slowly and incompletely soluble in water, but insoluble in alcohol. It is hygroscopic, and when exposed to the air for some time loses its value; hence it should be preserved in well stoppered bottles. Dilution with sugar of milk seems to retard deterioration, and saccharated pancreatin has been found to retain its peptonizing value better than the pure article. Dissolved in water, pancreatin yields a clear, pale yellowish liquid, which is precipitated by heat, mineral acids, metallic salts, absolute glycerin, strong alcohol, and tannic acid, but not by a saturated solution of sodium chloride; in this latter respect it differs markedly from pepsin. It is not possible to prepare a solution of pancreatin which will retain the activity of all the enzymes present: this is perhaps due to the destructive effect of the trypsin upon the other ferments. Pancreatin is incompatible with acid pepsin solutions, and hence they should not be combined. In dry form the enzymes of pancreatin are very stable, but in solution, neutral or alkaline, they undergo change even at ordinary temperature.

The Pharmacopœia requires that official pancreatin shall be obtained from the fresh pancreas of either the hog or the ox and that it shall be capable of converting not less than 25 times its own weight of starch into soluble carbohydrates. The presence of fat is limited to 3 per cent., which is determined by extracting 2 Gms. of pancreatin with three successive portions (20, 10 and 10 mils. (or Cc.) of ether in a stoppered flask, evaporating the combined ether solutions spontaneously and drying the residue to constant weight at 100° C. (212° F.).

The proteolytic value of pancreatin is determined by its action on milk, as directed in the Pharmacopœia; complete peptonization must be effected in 30 minutes at a temperature of 40° C. (104° F.). Its starch converting power is ascertained by allowing 0.3 Gm. of pancreatin to act on a mucilage of starch, made of 7.5 Gms. of dry potato starch and 200 mils. (or Cc.) of water, for 5 minutes at a temperature of 40° C. (104° F.), when a clear liquid should result which yields no blue, red or violet color upon addition of a few drops of tenth-normal iodine solution.

Pepsin.—This enzyme was discovered in 1836, by Schwann, after Eberle had furnished proof that digestion of food in the stomach is due neither to the mechanical action of the mucous membranes nor to the solvent action of acids, but is dependent upon some unorganized ferment present in the gastric juice; it was named pepsin, from the Greek word πέψις (digestion). Pepsin is a secretory product of certain glands embedded in the tissue of the inner coating of the

stomach, but has also been found in muscular tissue, urine, brain, and the mucous membrane of the intestines. True or active pepsin probably does not exist at all times in the gastric juice, but is formed by the action of hydrochloric acid and chlorides from a mother substance known as *pepsinogen*, as the digestive functions of the stomach may require; in support of this theory it has been found that glycerin will abstract increased quantities of pepsin from the mucous membrane of the stomach after this has been treated with 0.2 per cent. hydrochloric acid or 1 per cent. sodium chloride solution. The use of pepsin in medicine is mainly due to the efforts of Dr. Corvisart, court physician to the Emperor Napoleon III., but the quality of the commercial article has been vastly improved since that time; to the perseverance and energy of American pharmacists are due the improvements in the mode of manufacturing pepsin and the wonderful increase in digestive power of the commercial article.

In this country two kinds of pepsin are manufactured, known respectively as precipitated pepsin and soluble or scale pepsin; the former is made by the method recommended by E. Scheffer in 1872, which consists in precipitating an acid infusion (prepared cold) of clean mucous membrane of hog stomach by a saturated solution of sodium chloride, redissolving the precipitate in acid water, reprecipitating with salt in order to purify the pepsin, and finally drying at or below 40° C. (104° F.). A full account of this process may be found in the *American Journal of Pharmacy* for 1872. The process for the manufacture of the so-called scale or peptone pepsins insures an increased yield of product and higher digestive power, but not always the same degree of purity; it consists in subjecting the well-cleaned mucous membranes of animal stomachs, after being thoroughly minced by machinery, to a process of self-digestion in water acidified by hydrochloric acid at a temperature of 38°–45° C. (100.4°–113° F.), until the whole mass is converted into a uniform, transparent, glairy fluid. This is allowed to cool and deposit over night, after an addition of chloroform or sulphurous acid solution which prevents putrefaction and in no wise interferes with the activity of the pepsin; the liquid is carefully strained, concentrated in a vacuum apparatus to a syrupy consistence, and spread upon plates of glass, where it is allowed to scale in suitable dust-free rooms. Pepsin thus prepared always contains mucus, peptones, and syntonin, while that prepared by the Scheffer method is contaminated with salt and some inert albuminous matter. In 1891 a process was patented in this country and in England, combining the advantages of the two preceding processes. The essential features are as follows: The well-cleansed and minced mucous membranes are brought to solution by digesting with acidulated water, the solution being clarified after the addition of sulphurous acid; the clear liquid is separated from the deposit and then precipitated by saturating, at higher temperature, with sodium sulphate, whereby the pepsin is deposited, while the peptone remains in solution. The precipitated pepsin is dissolved in weak hydrochloric

acid and subjected to dialysis, which removes the sodium sulphate and remaining peptones, after which the residual solution is concentrated at a low temperature and dried on plates of glass. The sodium sulphate is not lost in the process, but reclaimed from the peptone solution by recrystallization. While the U. S. Pharmacopœia recognizes only the pepsin obtained from the glandular layer of fresh hog stomachs, and capable of digesting not less than 3000 times its own weight of freshly coagulated and disintegrated egg albumen in 2½ hours at a temperature of 52° C. (125.6° F.), when tested by the official process, the British Pharmacopœia admits pepsin from the stomachs of hogs, sheep, and calves, provided one part is capable of dissolving 2500 parts of hard boiled egg albumen at a temperature of 40.5 ° C. (105° F.) in the course of six hours.

French pepsin is chiefly obtained from sheep stomachs, and Boudault's preparation contains starch and sometimes lactic acid. The German Pharmacopœia does not prescribe the source of official pepsin nor the manner of its preparation; the stomachs of hogs and calves are, however, usually employed. Official German pepsin is required to dissolve 100 times its weight of hard boiled egg albumen in one hour, at a temperature of 45° C. (113° F.).

Pepsin exposed on a watch-glass to the air, even in damp weather, should not become sticky in the course of a few hours, showing the absence of an undue amount of peptone. It should form, with 50 parts of distilled water, an almost clear solution, which is not rendered turbid by the addition of acetic acid, showing the absence of mucus. (Pepsin made by Scheffer's process never yields a perfectly clear solution with water, owing to the presence of syntonin or acid albumin.) It should be free from any disagreeable or ammoniacal odor due to the presence of putrescible matter. A drop of tincture of iodine added to a solution of pepsin should not develop a blue or purplish-red color, showing the absence of starch and dextrin.

The greater the proportion of peptone present in pepsin the more rapidly does it absorb moisture from the air, and the greater the absence of mucus the less unpleasant will be the odor and the more perfectly clear will be the solution of pepsin in water, especially if the water be acidulated with acetic acid. Except in minute quantities, sodium chloride impairs the activity of pepsin; the same is true of alcohol. An aqueous solution of pepsin will decompose in a short time; after addition of hydrochloric acid it remains clear, but gradually loses its effect on albumen. Glycerin, on the other hand, preserves its virtues. Tannin and the alkali carbonates and bicarbonates inhibit the proteolytic action of pepsin. In the dry state pepsin is not injured when heated to a temperature of 100° C. (212° F.), but its aqueous solution loses its activity at a temperature above 70° C. (158° F.).

Saccharated pepsin, prepared by intimately mixing one part of pepsin with nine parts of sugar of milk, is a convenient form of administering small doses of pepsin to children.

Rennin, also known as *Chymosin.*—This milk-curdling enzyme, occurs in the stomach and the pancreas of animals, but the two substances do not appear to be identical. It is not recognized in the Pharmacopœia, but the *National Formulary* defines it to be the partially purified enzyme obtained from the glandular layer of the stomach of the calf and requires that rennin shall be capable of coagulating not less than 12,500 times its own weight of normal, fresh cow's milk.

Rennin in all probability is not always present in the stomach, but, like pepsin, is formed from a zymogen or mother-substance, designated as chymosinogen, by the action of hydrochloric acid. Definite information is not available as to the manner of obtaining rennin, and the statement of various authorities differ considerably.

It occurs on the market as a grayish-white or yellowish-white powder, or in grains or scales, having a peculiar odor and a slightly saline taste; sometimes excessive quantities of salt are found present. As rennin is hygroscopic and deteriorates rapidly upon exposure, it should be kept in well stoppered, amber-colored bottles in a cool, dry place. When added to water or diluted alcohol, it is taken up slowly, forming somewhat opalescent solutions.

For the purpose of determining the proper activity of rennin, the *National Formulary* directs that 0.004 Gm. dissolved in water shall be able to convert 50 mils. (or Cc.) of fresh milk into a firm curd in 37.5 seconds at a temperature of 43° C. (109.2° F.).

Desiccated Hypophysis, also known as *Desiccated Pituitary Body.*—The pituitary gland, located at the base of the brain, consists of two portions or lobes, the anterior or larger, and the posterior or smaller portion. Both lobes are ensheathed in a capsule derived from the dura mater, and are connected by a stalk, which is ordinarily solid but is sometimes found to be hollow. Extracts from the two lobes have been found to possess opposite or dissimilar properties, and only the smaller or posterior lobe is recognized officially, the Latin name *Hypophysis Sicca* being applied to it.

The Pharmacopœia defines the official desiccated hypophysis to be the posterior lobe of the pituitary body of cattle, cleansed, dried and powdered, and describes it as a yellowish or grayish, amorphous powder, having a characteristic odor, and partially soluble in water.

A solution of the water-soluble principle or principles from the fresh posterior lobe of the pituitary body of cattle is officially recognized as *Solution of Hypophysis* or *Solution of the Pituitary Body* (Latin name—*Liquor Hypophysis*). It is obtained by extracting the finely minced material with slightly acidulated water, boiling the solution for ten minutes and filtering; the filtrate is then sterilized and preserved in sterilized glass containers. It occurs as a transparent liquid, colorless or nearly so, and having a faint odor.

The chief action of the pituitary body seems to be an increase of the blood-pressure and contraction of involuntary muscles.

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